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## UTOPIAN OBSTETRICS\*

A PLAN PROMOTING EFFICIENCY TO THE OBSTETRICIAN AND SERVICE TO  
THE PATIENT

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**I**T happens to be our peculiar lot to live in an age of which there has been none other of equal importance to man's welfare. To win the war and preserve our way of life overshadows every other consideration; yet, no one doubts that another all-out effort will be necessary to win the peace.

In this hoped for period of reconstruction, it is my belief that something should be done to bring to the average physician, and the obstetrician in particular, a more deserved participation in a more abundant life.

There is deep significance behind the facts brought out by Falk in a recent paper entitled "Coronary Sclerosis, the Doctor's Disease."<sup>1</sup> From a study of statistics, he found that coronary disease killed doctors twice as often as laymen. While coronary deaths have increased 114 per cent among all men over a seven-year period, they have increased 240 per cent among physicians. There has been a 50 per cent increase in cardiac deaths among physicians between 1930 and 1940, but, contrasted with this increase from general cardiac causes, is an apparent 600 per cent increase in coronary types.

One cannot explain away these figures simply on the basis of greater diagnostic acumen. The increased susceptibility of the doctor may be

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due partly to greater strain and responsibility, irregular rest and eating habits, and greater physical, mental, and emotional hazards. To counteract these tendencies and possible influences, emphasis is put on moderation, equanimity, and the conservation of energy through the middle and later decades of life.

Falk emphasizes that the only compensation for normal fatigue is rest and that it is more important to get an adequate consecutive number of hours' rest than a number of irregular periods of rest. The doctor should not only have ample vacation periods, but also brief periods of complete physical and mental relaxation from the pressure of daily routine. He speculates on just what influence the replacement of man's former necessity for walking may be having on the increase in coronary disease.

Considering the long and expensive years of preparation for the practice of medicine and the fact that the physician has, through years of experience, attained his maximum efficiency and usefulness at the age when coronary disease takes its greatest toll, it is a matter of local and national concern that the public, if for no other reason than its own interest, should modify its time-honored concept of the busy doctor's daily life in order that some of these predisposing causes of coronary disease may be removed.

It would be of interest if the statistics gathered by Falk could be broken down still further to determine which of the specialties in medicine most favored the development of coronary disease. The specialty of obstetrics permits, least of all, avoidance of the factors which predispose to this disease. It is said that one of the most important attributes of the obstetrician should be equanimity, and rightly so, when one considers the need of a calm demeanor to counteract the fears of the patient's family and friends. Whatever benefit equanimity may be to the obstetrician, it would seem to be more than offset by the detrimental effect of many influences peculiar to this specialty.

Nature intended that man should get adequate hours of sleep and rest to remove waste products, repair tissue damage, and restore vitality. The necessity for this is recognized, and in practically all vocations, provision is made to insure that hours of labor shall not interfere with this fundamental need.

How goes it with the obstetrician? For some peculiar reason the majority of labor cases gets under way between the hours of bedtime and daylight and if accommodating enough to begin during the day, seldom fails to delay the hour of retiring. If he has been fortunate to have obtained full rest the preceding night, he is not only able but willing to lose sleep and spare no effort to render ideal service. However, the following day's office and outside work lack something of the necessary efficiency due to loss of sleep. The onset of another labor ruins the expectation of hoped-for sleep the following night. To obtain much-needed rest, he must depend on the less mature judgment



of an interne or nurse to supervise progress and determine the ideal time for sedation or interference. If the case extends on into the day, office hours and outside work are disrupted. Cancelled office visits may involve failure to recognize developing toxemia or perform a necessary external version, which are equally as important as the labor, although not so recognized by the patient or family. Cancellation of prenatal visits and postponement of office work entail much inconvenience and waiting to the patients. Should a third successive night's sleep be lost, this patient not only receives inferior service in labor, but the office work receives inferior attention.

Loss of sleep and excessive tiring lower the physician's resistance, increasing his susceptibility to disease and infection. Vacations are too easily postponed. The post-partum patient, coming for her final examination, is over-solicitous concerning her physician's need of a vacation, but the prenatal patient is equally insistent that he be available at the expected date of confinement.

There is need of some practical workable compromise between the laity's concept of an obstetric attendant who must be available, not only around the clock, but also around the calendar, and a plan of obstetric care which will assure the obstetrician definite hours of sleep, recreation, and regular vacations.

Such a plan had been devised and was about to be put into operation by several of us when the present requirements of national defense necessitated postponement, through loss of personnel. For the purposes of this presentation it is unfortunate that we are therefore unable to actually state our experience with what we choose to call "Utopian Obstetrics," but the plan is to be put into effect at the earliest opportunity.

One may appreciate better the fundamental requirements of such an organization if he will trace the evolution of a growing obstetric practice. To paraphrase a Biblical narration: The seven years of famine are succeeded by the seven years of plenty, after which further increase in work causes the obstetrician to ask himself why he ever aspired to a busy obstetric practice anyway. He takes unto himself an associate, who, because he is made of the right stuff, is before long in the same predicament.

We now have an association of two specialists, neither of whom is getting sufficient sleep, recreation, or vacation, nor is the one physically able to take over for the other in respect to office work or any of the above-mentioned necessities. Each one lives in constant fear that the other may be disabled by sickness or accident, and realizes, only too well, the physical impossibility of taking over the additional practice.

It is admitted that in less populous areas, the problem may not be such a pressing one, but, even so, it still carries with it the same peculiar disadvantages. The raising of fees offers an effective escape from

overwork but it seems unwise to overstep what the laity regard as reasonable remuneration even for a specialist. Furthermore the obstetrician owes it to himself to retain a sufficient volume of practice to insure wide experience and safeguard himself against periods of economic depression.

It seems to us the solution lies in forming a group, the nucleus of which should be one or two men who control a considerable volume of work. An association of four men in a populous center lends itself to a convenient division of labor. Among the basic requirements there should be congeniality, a spirit of "give and take" flexible enough to smooth over differences of opinion, frankness, honesty, and a willingness to sacrifice some degree of independence and possibly some individual income for the larger benefits to be obtained through such an association. Through free expression of opinion, a standardization of procedure will gradually be evolved. It is essential that the group work exclusively in one institution and that the offices be in or adjacent to the hospital and be easily accessible.

In arranging a rotation of hours, provision must be made for (1) office hours, (2) hospital work, (3) outside work, and (4) definite hours for sleep and recreation.

During the morning hours, two of the group work at the office; the third member remains in the hospital supervising labors, and making rounds, while the fourth member attends to outside work, whether this be teaching, clinics, home calls, or emergencies, but with more or less of the time free for personal use. In the afternoon the two members at the office shift to hospital and outside work, respectively, while the two previously attending to these duties, shift to the office.

At night, one member remains available at the hospital for labor cases until 1:00 A.M.; he is then relieved by another who remains on duty until the day shift begins. This insures considerable rest for these two members. Since outside calls and emergencies are relatively less at night, the other two members are able to use this time for rest or other purposes with little chance of interference. All telephone calls from patients at night are taken by the member on duty at the hospital.

The shifts vary from day to day and week to week. It is possible for the members to have more free time at week ends, since shifts of hours then apply only to duty at the hospital and responsibility for outside calls or emergencies. It is also possible to cover the work with three men, permitting one member of the group to be absent several days to a week each month for recreation or visiting other clinics in search of improved methods.

From the patient's standpoint, what objections may be raised to this manner of obstetric practice? First and foremost, the patient may feel she cannot exercise the privilege of calling upon the physician of her choice. This will be obviated by the fact that during the prenatal period she will contact each member of the group sufficiently often to feel well acquainted with and have confidence in each one of them. If unusual complications arise during pregnancy or labor, she may still designate

the one whom she would prefer for consultant or assistant. But unless this privilege is restricted to occasions of real importance, the plan loses its benefits to both the patients and the group members.

The benefits to the patient far outweigh the disadvantages. At the office, appointments are kept on time, much to the betterment of the patient's disposition and the satisfaction of those who may have brought her to the office. The patient is impressed by the fact that the doctor seems to have ample time to examine her thoroughly and answer her questions in an unhurried manner. She does not have to experience the inconvenience of leaving the office without being seen, due to a hospital or outside emergency which suddenly interrupts office hours. Furthermore, she feels her office visit is more worth while if the doctor is alert and wide-awake, than if he is nodding or momentarily dozing in her presence.

At the hospital, each shift during labor brings to the patient the advantage of consultation, as agreement is reached on what procedure or treatment will best serve the mother's and baby's welfare. By analogy this practice has been an accepted procedure in the nursing care of patients for many years. Indeed, the patient would be one of the first to object if twenty-four-hour duty was imposed on her nurse.

From the doctor's standpoint what objections may be raised to this manner of obstetric practice? Objections will arise unless the members composing the group are congenial, conscientious, honest, and able to instill confidence in patients. Each member should be well grounded in the basic fundamental principles of obstetrics and able to standardize on the details as well as the essentials of prenatal care. Harmony of this degree could perhaps be attained more successfully if the members of the group received their training from the same clinic or under the same Chief.

Some would consider the division of income as the greatest difficulty to surmount. It is not my intention to present in detail a financial set-up that would meet with universal approval. Suffice it to say that one cannot have his cake and eat it too.

The rewards of longer, more enjoyable and abundant life, opportunities for recreation, rest, travel, study, research, visiting, and learning from one's contemporaries, and last, but not least, the knowledge that patients can be treated more satisfactorily, far outweigh the question of whether one might do better financially by practicing alone. On these premises, it should not be difficult for a group to divide, on a percentage basis and with due regard to seniority, what remains after routine office expenses have been paid.

Such a plan of practice would seem applicable not only to obstetrics, but to pediatrics, surgery, and other specialties. It would seem highly desirable in general practice in which obstetric cases and emergencies

so frequently disrupt office hours. Confidence in the individual physician would be replaced by confidence in the group as a whole.

Even as these lines are written, there are heartening signs that the greater resources and gathering strength of the nations opposed to the Axis Powers are gradually turning the tide. There is a prevailing confidence that the war will not only be won but the peace also, and that we will live in a better world. There will be many changes in our order of living, some of which will certainly concern the practice of medicine. We should proceed on the concept of the greatest good to the greatest number, stress the importance of medical counsel in attaining this end through any legislative means, and finally strive for a better adjustment between the work to be done and the life to be lived as visioned in Utopian Obstetrics.

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### DETAILED TECHNIQUE OF A MODIFIED LOCAL ANESTHESIA FOR CESAREAN SECTION\*

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FOR the past twenty years we have been doing cesarean sections under local anesthesia at the Long Island College Hospital. At first very few were successful. Oftentimes they were more vocal than local, in that the patient complained vociferously, or an incessant chattering by an attendant was necessary to distract her attention. Because of its many advantages, however, we persisted until we now have a satisfactory technique, which is used routinely for all cesarean sections.

Under procaine anesthesia temperature and pain sensation are lost before the sensations of touch and pressure disappear. For this reason the patient often feels the manipulations of the operator without experiencing any pain. In order that her anxiety may not be increased, the tissues are handled as gently as possible and wide retraction is avoided. Adhesions are severed with a knife and not separated by blunt dissection. Unnecessary traction on the uterus, sutures, and clamps is never permitted. Because the manipulations required for the removal of the child and the placenta are too vigorous for many local anesthetics, brief analgesia is induced with nitrous oxide while these manipulations are carried out.

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Unfortunately the drugs which usually are relied upon to relieve the patient's anxiety when local anesthesia is employed, cannot be given preliminary to a cesarean section because of their effect on the child. After the operation is started and shortly before the child is removed from the uterus, one-third of a grain of pantopon and  $\frac{1}{200}$ th of a grain of scopolamine are given for this purpose. Because vomiting occasionally follows the use of morphine, pantopon is preferred.

To obtain the maximum effect with a minimum of drugs three different solutions are used.

Solution 1 consists of 50 c.c. of  $\frac{1}{2}$  per cent procaine without adrenalin. It is employed for the intradermal and subcutaneous infiltrations which anesthetize the site of the incision. Because slight sloughing sometimes occurs when adrenalin is used in these intradermal injections and because prolonged anesthesia in this region is secured by the subsequent deeper nerve blockings, adrenalin is omitted from this first solution.

Solution 2 is prepared by adding 1 c.c. of 1-1000 adrenalin to 200 c.c. of 1 per cent procaine. This 1 per cent procaine and 1-200,000 adrenalin solution is used only for the deep nerve-blocking injections which are made in the vicinity of the semilunar lines at the outer border of the recti muscles. By blocking the nerves before they give off their terminal branches, these injections anesthetize the entire thickness of the abdominal wall from the skin to the peritoneum inclusive. In its action on nerve fibers, procaine affects the smaller relatively thinly medulated fibers more readily than it does the larger more thickly medulated nerves. For this reason a  $\frac{1}{2}$  per cent solution is less efficacious in blocking the larger nerve elements which are adjacent to the lineae semilunares.<sup>1</sup>

Solution 3 is made up of 50 c.c. of  $\frac{1}{2}$  per cent procaine to which  $\frac{1}{4}$  c.c. of 1-1000 adrenalin is added. It is used to infiltrate the peritoneum on each side of the bladder and over the lower part of the uterus. If at any time in the course of the operation additional injections are required, this solution rather than the stronger one is selected. Should the anesthesia wear off by the time the abdominal incision is to be closed, the peritoneum is infiltrated with Solution 3 before it is sutured. Additional injections into the fascia and skin seldom are necessary.

Although it is well known that the addition of adrenalin prolongs the anesthesia produced by procaine, the effect of various dilutions of this adjuvant is somewhat different than might be expected. Hirshfelder and Bieter have shown that 16.6 minutes of anesthesia produced by procaine alone may be prolonged to eighty-three minutes by adding 1-50,000 adrenalin and that it may be prolonged still further to 89.2 minutes by diluting the adrenalin solution to 1-200,000. From Table I it may be seen that the greatest prolongation of the anesthesia and the least danger of toxic symptoms may be obtained by the use of a 1-200,000 solution.<sup>2</sup>

#### DANGERS

The lethal dose of procaine used in the manner described is unknown for man. In the guinea pig, rabbit, and cat it averages 430, 460, and



450 mg. per kg. of body weight.<sup>1</sup> If human susceptibility is similar to that of these laboratory animals, at least 25 Gm. would be required to kill a woman weighing 130 pounds. When the drug is injected into a vein, however, only 50 mg. per kg. are required to cause death in the same animals. Its toxicity accordingly is increased almost tenfold whenever procaine is introduced directly into the circulation. The greatest dangers which accompany the use of this drug therefore are its accidental injection into a vein and its rapid absorption in very vascular tissues. Because the tissues injected in our technique are relatively avascular, the latter danger is very slight unless the needle is unintentionally passed into the substance of the rectus muscle in the vicinity of the deep epigastric vessels. The risk of introducing the solution directly into a vein also is slight if the needle is kept moving throughout the injection. As an added precaution, the plunger should be withdrawn slightly before the major portion of the injection is forced into the tissues in order that the entrance of the needle into a vein may be revealed by the presence of blood in the syringe.

TABLE I. DURATION OF PROCAINE ANESTHESIA (HIRSHFELDER AND BIETER)

EPINEPHRIN CONTENT	MINUTES OF ANESTHESIA
0	16.6
1-500,000	83.0
1-100,000	87.2
1,200,000	89.2
1-500,000	65.4.

While the supposed lethal dose may be as large as 25 Gm. for the average person, less than one-tenth of this amount of procaine may cause toxic manifestations. These include nervousness, anxiety, talkativeness, tremor, nausea, vomiting, and a fall in blood pressure. As most of these symptoms also follow the use of adrenalin, some of the unsuccessful results of local anesthesia which are attributed to an unsatisfactory choice of patients or to the employment of a faulty technique, probably are due to the use of too much of one or both of these drugs. According to the majority of writers not more than 1 to 1½ Gm. of procaine and 15 min. of adrenalin should be used. We formerly exceeded these amounts in some cases and the toxic manifestations mentioned militated against a good result. At present we are able to obtain satisfactory anesthesia within the recommended limits.

#### TECHNIQUE

All injections are made with a 10 c.c. syringe to which lateral and plunger rings are attached to facilitate backward and forward movement of the plunger. This type of syringe is preferable to the various constant flow devices since the latter offer no means of determining whether a vein has been entered. Twenty-five gauge three-fourths-inch needles are used for the skin and 22 gauge 3-inch ones for the deep injections.

The point of the needle is introduced into the skin slightly to the left of the midline and a small amount of  $\frac{1}{2}$  per cent procaine without adrenalin (Solution 1) is injected intradermally. The needle is then plunged through the skin and 1 c.c. of the solution is forced into the subcutaneous tissues. As anesthesia is almost immediate within the

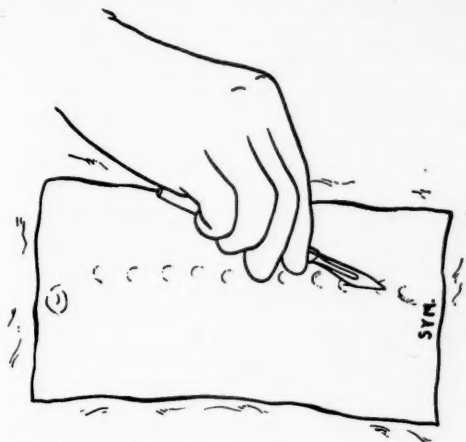


Fig. 1.—Incision of the skin through the line of intradermal wheals.

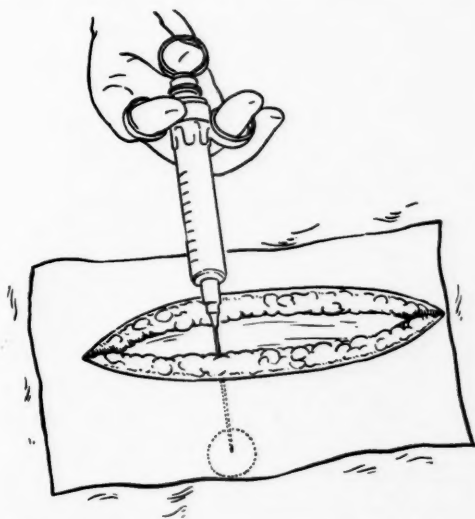


Fig. 2.—Deep injection to block the nerves. The needle is introduced at the junction of the fascia and subcutaneous tissues and the injection is made in the region of the semilunar line.

intradermal wheal, the needle is painlessly reintroduced near its periphery and a second wheal and subcutaneous injection are made. These intradermal and subcutaneous injections are repeated until they extend somewhat beyond the extremities of the purposed line of incision (Fig. 1). About 25 c.c. of Solution 1 are required for this purpose.

Following a brief delay to allow for complete anesthesia, the skin and subcutaneous tissues are incised down to the fascia over the rectus

muscle. A 22 gauge 3-inch needle is then introduced into the incised tissues as near as possible to the fascia and passed outward to the outer border of the right rectus muscle. After testing to determine whether a vein has been entered, 2 c.c. of 1 per cent procaine in 1-200,000 adrenalin (Solution 2) are forced into the region adjacent to the linea semilunaris (Fig. 2). Similar injections are made at intervals of 1 cm. on each side of the wound as shown in Fig. 3. At the upper and lower angles, the needle is passed obliquely in order that the injections may

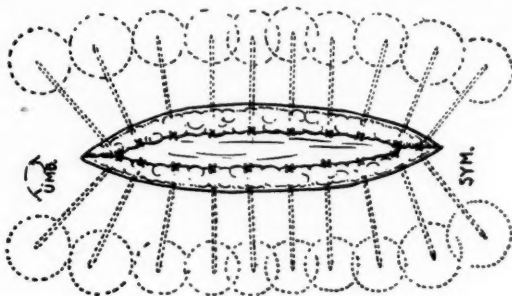


Fig. 3.—Diagrammatic representation of the wheals produced by the deep injections.

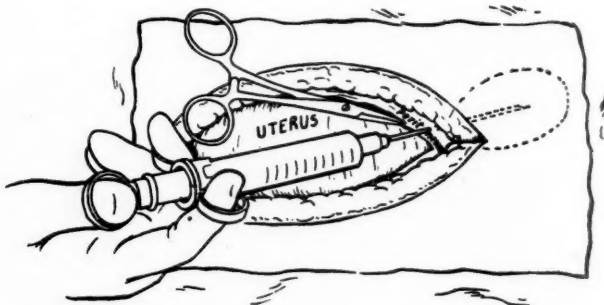


Fig. 4.—After making traction on the peritoneum, 5 c.c. of Solution 3 are injected into the subperitoneal tissues on each side of the bladder.

extend beyond the limits of the incision. A slightly larger amount of the solution also is introduced into these areas. Cross section of the abdominal wall in the region described shows the ease with which fluid placed near the linea semilunaris may diffuse through the fascia and reach the nerves which pass inward between the transversalis and internal oblique muscles to pierce the rectus sheath. If the injections are made correctly, a continuous mass of 1 per cent procaine is placed along this area on each side of the incision in order that it may infiltrate through the fascia and block the nerves before they give off the terminal branches which supply the abdominal wall from the peritoneum to the skin.

At this stage an attendant is requested to note the time and tell the operator when ten minutes have passed. As this interval is necessary for the blocking of the nerves, the operator must wait the full ten minutes before continuing the operation. Since the ligation of the superficial vessels is the only thing that can be done in the interval, this wait-

ing period is the most difficult part of the procedure. The success or failure of the local anesthesia, however, depends upon its strict observance.

After the required time has elapsed, a small incision in the fascia is made with a knife and this is enlarged with seissors. Scissors are used because they may cause slight discomfort in imperfectly anesthetized tissues which otherwise might be incised painlessly with a knife. Should

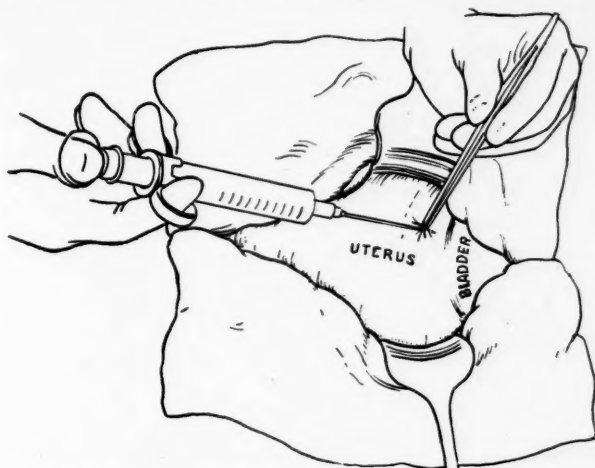


Fig. 5.—After picking up the peritoneum with smooth pointed forceps, 10 c.c. of Solution 3 are injected beneath the bladder reflection.

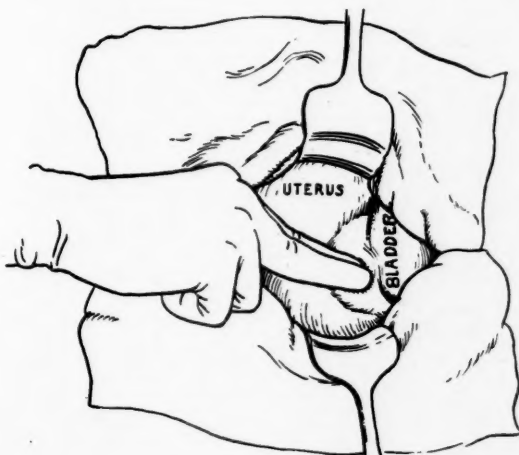


Fig. 6.—Pressure over the wheal causes the dissemination of the solution beneath the bladder and its reflection.

their use show the anesthesia to be imperfect, a slightly longer interval of waiting is indicated. Following this, further procaine is required if the sensitiveness is not eliminated. On the other hand, an absence of discomfort when the scissors are used is indicative of perfect anesthesia, and the operator may proceed with the assurance that even the peritoneum may be incised without pain.

The inner margin of the rectus muscle is separated from its sheath and the peritoneum is exposed. During this step of the operation, slight traction on the fascia is made with clamps to facilitate the dissection and reveal any possible inadequacy of the anesthesia.

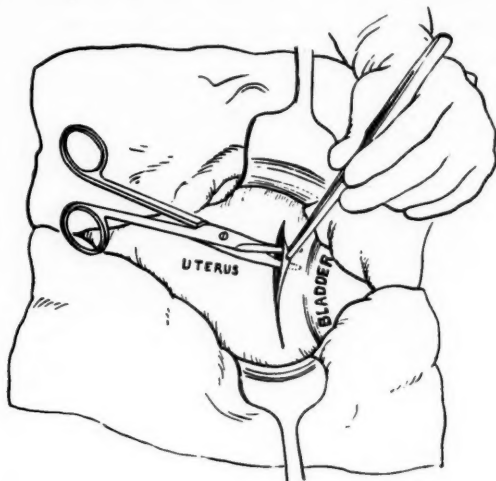


Fig. 7.—After making the transverse incision through the peritoneum, the closed Mayo scissors are introduced on one side of the midline then opened and withdrawn.

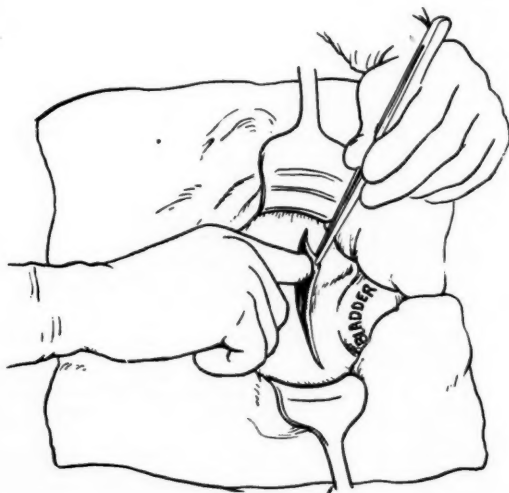


Fig. 8.—The finger is introduced into the area dissected free by the scissors and by a side-to-side movement completes the dissection. By the same technique the bladder and its reflection are dissected through on the opposite side.

The peritoneum is then grasped with clamps and incised. If the nerve block is satisfactory, as it usually is, this can be done without further use of procaine. If it is not, the clamps will cause discomfort and the peritoneum should be injected with  $\frac{1}{2}$  per cent procaine and 1-200,000 adrenalin (Solution 3) before the incision is made.



After incising the peritoneum, traction is made on one side at the junction of its middle and lower third and 5 c.c. of Solution 3 are injected into the subperitoneal tissues on that side of the bladder (Fig. 4). This is followed by a similar infiltration on the opposite side.



Fig. 9.—After the flaps have been prepared and before incising the uterus one-third of a grain of pantopon and 1/200th of scopolamine are given. The uterus is incised in the midline with a knife and the incision thus made is enlarged with scissors. During this procedure nitrous oxide (85 per cent) is given for one minute. The hand is introduced into the uterus and acting like a vectus assists in the delivery of the child's head. Forceps are very seldom used. During the delivery of the child nitrous oxide is continued but is not given for much more than one minute.

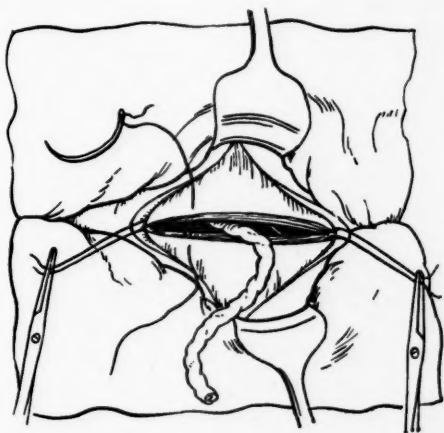


Fig. 10.—Deep interrupted sutures are introduced through the entire thickness of the uterine muscle down to the endometrium. While these interrupted sutures are being introduced, the placenta is not disturbed.

Smooth-pointed forceps now pick up the peritoneum on the anterior surface of the uterus about 1 inch above the bladder, and 10 c.c. of 1/2 per cent procaine and 1-200,000 adrenalin (Solution 3) are injected beneath the bladder reflection (Fig. 5). Pressure on the wheal thus made, disperses the fluid toward the sides and under the bladder (Fig. 6).

The peritoneal reflection is incised transversely and scissors are passed beneath on one side, opened, and withdrawn (Fig. 7). Into

the space thus formed the finger is introduced and by a side-to-side motion dissects off the peritoneum and bladder from the lower segment and cervix (Fig. 8). After repeating this step on the opposite side, the adhesion in the midline is cut and the bladder is pushed off from the uterus.

If advisable, an upper flap is prepared similarly by blunt dissection.

Before the uterus is incised one-third of a grain of pantopon and 1-200th of scopolamine are given and the administration of nitrous oxide is started. During this time the uterus is incised with a knife and the incision is enlarged with scissors. The child is removed head first manually and the nitrous oxide is then discontinued (Fig. 9). Nitrous oxide is given for a very short interval only, not much over one minute, and produces analgesia without anesthesia since the patient usually hears the first cry of the child. If the nitrous oxide is given

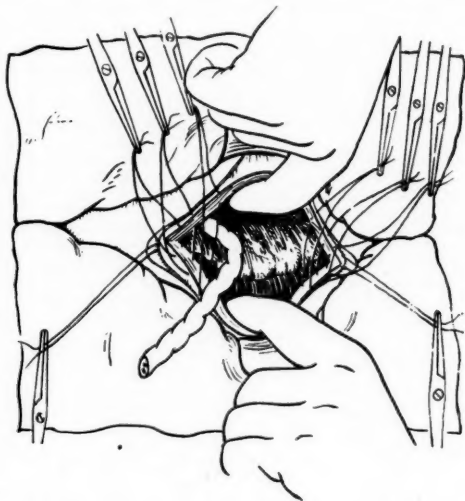


Fig. 11.—After introducing all of the deep sutures, the uterine wound is spread apart and the placenta is removed manually. Following the removal of the placenta, the uterine wound is temporarily closed by making traction on the clamps which hold the deep sutures and the sutures are then tied individually. While the placenta is being removed, nitrous oxide 85 per cent is again given for about one minute.

over too long a period, the patient may become restless and force the intestines into the field of operation. Immediately after the delivery of the child, 1 c.c. of ergotrate is injected hypodermically and interrupted sutures are introduced through the muscle down to the endometrium (Fig. 10). These sutures are placed  $1\frac{1}{2}$  cm. apart and are left long. After they have been introduced throughout the length of the wound, nitrous oxide is again administered for about one minute. The wound is then spread apart so that the hand may be introduced for the removal of the placenta (Fig. 11). The placenta is separated and removed manually. Immediately after the removal of the placenta, the nitrous oxide is discontinued. Here again it is important that the administration of the gas be as brief as possible in order that the patient may not get out of control.

The uterus is closed by making traction on and tying the previously introduced sutures. By waiting a few minutes before removing the

placenta, the uterus becomes retracted and is better able to control bleeding from the placental site than it is when the placenta is removed immediately. Additional sutures are introduced wherever necessary. The upper flap is brought down over the upper angle of the uterine wound and following this the lower flap is brought up over the upper one and sutured (Fig. 12).

Some patients go to sleep soon after the placenta is removed. Most of the others are quiet and free from anxiety.

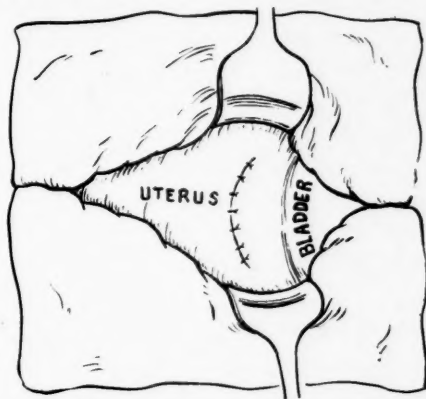


Fig. 12.—The uterine wound is closed and covered with peritoneum. If the parietal peritoneum is sensitive when it is sutured, a small amount of Solution 3 should be injected into the subperitoneal tissues adjacent to it.

The abdominal wound is closed in layers. This usually can be done without further anesthesia. If the anesthetic has worn off, however, the peritoneum is infiltrated with Solution 3 before it is sutured. It is not necessary to reanesthetize the fascia and skin.

The amounts of the various solutions generally required for the entire operation are shown in Table II. By using different dilutions, the quantities of procaine and adrenalin are considerably reduced. Only 1 to 1.3 Gm. of procaine and 9 to 11 min. of adrenalin are required in most cases. At the same time ample solution (120 to 160 c.c.) is available for all steps of the procedure.

TABLE II. AMOUNTS OF PROCAINE AND ADRENALIN USED

	C.C.	PROCAINE CONTENT GM.	ADRENALIN CONTENT MIN.
Solution 1	20-30	0.15	0
Solution 2	80-100	0.8-1	6-8
Solution 3	20-30	0.15	3
Total	120-160	1.1-1.3	9-11

#### ADVANTAGES

The chief advantage of local anesthesia lies in the fact that its use is accompanied by little or no immediate risk of death. I do not know of nor have I heard of a single instance in which death occurring during or immediately after a cesarean section was attributed to local anesthesia. I am unable to say the same for any other anesthetic agent.

Because of its safety many men select this type of anesthesia in cases of toxemia, respiratory infection, diabetes, heart and kidney disease. If it is best in these serious cases, it certainly should be best for the ordinary cases as well.

Under local anesthesia the contraction and retraction of the uterus is not interfered with as it is when general anesthesia is used. The tendency toward hemorrhage from the placental site during and immediately after operation is greatly diminished. This is an important advantage when the operation is done before the onset of labor or in the presence of uterine atony late in labor. The freedom from circulatory disturbance together with this lessened tendency toward hemorrhage greatly reduces the possibility of the occurrence of shock.

The general condition of the patient immediately after operation is so good and her convalescence is so much better than after general anesthesia that even the operators who have trouble in obtaining satisfactory anesthesia by means of the local technique are reluctant to discontinue its use.

Fluids can be taken by mouth before, during, and immediately after operation. Thirst accordingly either does not occur or is easily relieved. Sweating also is seldom observed and the dehydration which is so common after most major operations is greatly reduced or entirely eliminated.

Vomiting during and after operation does not occur unless excessive amounts of the drugs are given. As a result the stomach need not be empty at the time of operation. For the same reason aspiration pneumonia and plugging of the bronchia do not occur. Because the decision to operate often is made after labor has started and after food has been taken this freedom from gastric disturbance and its sequelae is one of the chief reasons for the selection of local anesthesia.

Foods are ingested within a few hours after the patient returns to her room. Because of this and because the intestines are seldom seen during the operation, distention and gas pains are much less frequent than after general anesthesia.

The heat regulating mechanism is not disturbed and abnormal sweating and chilling of the body surface do not occur.

Since the respiratory tract is not irritated as it is when inhalation anesthesia is used, the bronchial secretion is not increased and latent infection in the lungs is not activated. For this reason and because the absence of vomiting eliminates the possibility of aspirating gastric contents, pneumonia and massive collapse of the lungs seldom occur. The lack of respiratory irritation also makes possible the use of cesarean section in women who ordinarily would be considered poor risks because of the presence of an upper respiratory infection.

The gentle handling of the tissues required by the local technique coupled with the fact that the patient is active almost immediately after

the operation diminish the risk of thrombosis and embolism, postoperative complications which are not infrequent after ordinary cesarean section.

When this technique is followed, the child is not affected by either the analgesic drugs or the anesthetic agents. As a result, the child cries spontaneously as soon as it is taken from the uterus. Anoxia and respiratory difficulties, accordingly, are absent in all cases in which the child's condition is satisfactory at the beginning of the operation.

#### DISADVANTAGES

The only disadvantages are that it is time consuming, requires gentle handling of the tissues, and tries the patience of the operator. With practice it can easily be mastered and the satisfaction of achievement will then reward the surgeon for his perseverance.

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20 LIVINGSTON STREET

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### THE ETIOLOGIC AND PATHOLOGIC FACTORS IN A SERIES OF 1,741 FIBROMYOMAS OF THE UTERUS\*

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THE literature of fibromyomas of the uterus in the past ten years stresses etiology especially in regard to the reproductive hormones. One of the first to write upon this subject was Moench,<sup>1</sup> who in 1929 suggested the female sex hormonal influence upon the development of the tumors, based upon the observations that the tumors develop only during the active sex and reproductive life of the woman.

This theory was greatly amplified and given widespread appreciation by Witherspoon<sup>2-4</sup> in 1933 to 1935, who ably argued that the causative factor must be the estrogenic hormone. The main basic fact was the association of hyperplasia of the endometrium with fibromyomas, which he found to be as high as 55 per cent. This theory was supported by King.<sup>5</sup> These two also thought that chronic pelvic infection played a part in excess production of estrogens by ovarian congestion.

\*Read at the Fifth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Atlanta, Ga., February 6 and 7, 1942.



Since then there has been some dissent from these findings. Kanter, Klawans, and Bauer,<sup>6</sup> in a careful study of 100 patients with fibromyomas, found hyperestrinism to play a part, but not the only one in the etiology, and they conclude that various factors must be associated. They found endometrial hyperplasia in 55 per cent of 100 cases. Light<sup>7</sup> in 100 cases showed hyperplasia in only 17 per cent and Reis<sup>8</sup> in 18 per cent. Bowers,<sup>9</sup> in a study of 476 cases, reported endometrial hyperplasia in 11 per cent. Brewer and Jones<sup>10</sup> found it in only 1 per cent of 100 carefully studied cases. Henderson<sup>11</sup> found swiss-cheese type hyperplasia of the endometrium in 6.5 per cent of the uteri of 727 fibromyomatous patients.

These varying percentages of coincident hyperplasia may be due to different criteria of what is hyperplasia, an entity only recently widely introduced to pathologic study. Furthermore, the interpretation of the pathology of the endometrium may vary with the cyclic stage of removal.

In attempts to show the influence of estrogen on the production of fibromyomas, Nelson<sup>12</sup> injected 32 guinea pigs with various estrogenic substances over periods of two to ten months and was able in 6 cases to produce fibromyomatous growths in and about the uterus. These were associated with adenomatous hyperplasia of the endometrium with hemorrhage and metaplastic surface epithelial changes in the cervix with hyperkeratinization. The hyperplasia of the endometrium was made to disappear by injections of one-fifth to one-half rabbit units of progestin daily for ten days. Since the pioneering work of Nelson, a dozen or more papers have been published by Lipschutz, Vargos, and associates in Chile.<sup>13-20</sup> Their thoroughly documented and well-illustrated studies may be summarized as follows: Using large doses of various esters of estradiol, injections or pellets, they produced in castrated female guinea pigs fibrous growths, usually subperitoneally about the uterus or other organs in the abdominal cavity. If they used small doses they produced hyperplasia of the endometrium and metaplasia of the cervical mucosa. Neither of these conditions developed if the injections were intermittent. In order that the condition develop, the doses had to be given continuously. Prevention of the development of the new growths of hyperplasia was achieved also by simultaneous introduction of progesterone and testosterone. The growths were fibrous tissue only, not fibromyomatous, and usually were not in the myometrium. They occurred in the abdominal cavity, but never in the thoracic cavity.

Our study embraces 1,741 fibromyomas and the associated pathology found at operation in this community during the past twenty years. The 1920 census population was 60,211; the 1930 census, 60,342; the 1940 census, 65,919. The Department of Commerce reports 58 per cent white and 42 per cent Negro. The white population is essentially colonial English descent. Approximately 5 per cent of whites and 5 per cent of Negroes came here for operations from out of the city.

The pathologic study includes practically all of the operations done in the region during twenty years. Several pathologists have taken part in recording the observations, but the findings were carefully and fully

described and often illustrated by hand drawings. With the exception of adenomyosis, the incidence of the entities is quite uniform from year to year.

*Race Incidence.*—Of the 1,741 cases, 575 occurred in white women and 1,166 in Negroes. Since, in the ratio of white to Negro, the population here has been quite uniformly 58 to 42, the corrected ratio of incidence in the white to that in the Negro is as 479 to 1,457 or 1 to 3.3. The principal value of this study lies in those figures, for we know of no other where the essential factors are under such control. Most studies are made in large cities where the population is fluctuating, where certain economic strata of the population are concentrated at various hospitals, so that an accurate incidence cannot be ascertained. Miller,<sup>21</sup> in New Orleans, in 1924, concluded that fibromyomas were nine times as frequent in Negroes as in white women. He analyzed only 150 cases, and Lewis in the discussion dissented from this high incidence. Alsobrook,<sup>22</sup> in New Orleans, in 1931, in a study of 1,000 cases, estimated that the condition was five times more frequent in the Negro than in the white race. Cohen,<sup>23</sup> also of New Orleans, in 1930, analyzed 1,000 cases, 897 in Negro women and 103 in white. Levy,<sup>24</sup> in New Orleans, in a study of 5,821 patients operated upon for fibromyomas, found 12.2 per cent in white and 87.8 per cent in Negro women.

The greater incidence of the fibromyomas in the Negro women and their apparently more rapid growth may be associated with the greater tendency of keloid development in the Negro. (For the past five years here all of the post-operative keloid scars in gynecology patients have been recorded along with the reason for operation. It will be interesting to ascertain the coincidence of fibromyomas in those patients.) Along this same line there is a great tendency for development of large fibrous tumors in the Negro afflicted with lymphogranuloma. While it is true that white individuals have this infection, they seldom develop such tumors.

*Age.*—The youngest white woman was 18 years and the oldest white woman, 76 years. The youngest Negro woman was 17 years and the oldest Negro, 75 years. The greatest age incidence in the white patient ranged from 37 to 46 years inclusive and in the Negro patients from 29 to 42 years inclusive. The average age of the white woman in this series was 39 or 40 years, while that of the Negro woman was 36 or 37. This race relationship is identical to that found in a similar study of the incidence of eclampsia.

*Size of the Tumors.*—In the vast majority of cases the tumors were multiple. In most cases a record was made of the diameter of the tumors in centimeters. Five centimeters was the dividing line arbitrarily chosen to illustrate the size, large or small. Thus 301 white women had tumors smaller than the diameter of 5 cm., and 197 had tumors larger than 5 cm.; 302 Negro women had tumors smaller than 5 cm. while 586 had large tumors. In other words, 60 per cent of the white women had smaller than 5 cm. tumors and 40 per cent had large; 34 per cent of the Negro women had small tumors and 66 per cent had large. The Negroes had, then, not only three and one-third times the incidence, but they had  $1\frac{1}{2}$  times the incidence of the larger tumors.

*Pelvic Infection.*—In the 575 cases in white women, salpingitis occurred 93 times (16.2 per cent), while in the Negroes it was present in 633 cases (54 per cent) of the 1,166. Forty per cent of all patients operated upon for chronic salpingitis here had fibromyomas.

Moench and Witherspoon are of the opinion that the presence of infection and hyperemia have much to do with increased ovarian activity of estrogenic type, with tendency to suppression of the corpus luteum. However, in this study corpus luteal cysts were by no means absent. In the 575 white women there were found at least 67 follicular cysts and 43 luteal cysts. In the 1,166 Negro cases, there were at least 225 follicular cysts and 117 luteal cysts. Possibly more pathology of similar type may have been present in ovaries which were not removed. Brewer and Jones<sup>10</sup> found ovarian changes to approximate those found in normal pelvis. Adenomyosis began to be recorded only after 1926, but since then appeared quite uniformly year after year, there being 21 cases among the 575 white patients (3.6 per cent) and 18 among the 1,166 Negroes (1.5 per cent).

*Degeneration.*—Necrosis was found in 45 fibromyomas of the 575 white women (7.8 per cent) and in 190 tumors of the 1,166 Negro women 16.2 per cent. One would naturally suspect that the incidence of necrosis would be greater in the earlier reports when operations were deferred longer than in recent years. However, that does not appear to be the case in this series. Necrobiosis is the result of vascular changes usually on the venous side, so that congestion, hyperemia, edema, diapedesis and thrombosis are more common than anemic infarction. Pregnancy has long been known to be associated with red degeneration which is essentially incomplete interference with venous circulation, and no doubt pelvic infection has a similar effect. Rapidity of growth certainly ought to be accompanied by greater incidence of vascular degeneration. Consequently, the more frequent occurrence of necrotic changes in the tumors of Negro women is evident. Likewise, calcification, which is an end stage of necrosis, is more frequent in the Negro, occurring 50 times in the 1,166 cases and 14 times in the 575 white cases.

Pure myomas were found in 11 white patients and in 37 Negro patients. Adenomyosis of the uterine wall or of the fibromyoma occurred in 21 white women (3.6 per cent) and in 18 Negroes (1.5 per cent).

A record of the ovarian cysts revealed, in addition to the incidence of follicular and corpus luteum cysts, 11 cystadenomas in the white patients. Three of these were malignant. In the Negro patients there were 12 such cysts and 5 were malignant. Dermoid cysts of the ovaries occurred in nearly 1 per cent of the white patients (.5 cases) and in  $2\frac{1}{3}$  per cent of the Negroes (26 cases).

The following were rare complications: tubal pregnancy, 2; large cystic degeneration of the tumors, 2; ovarian fibromas, 2; solid ovarian carcinomas, 1; ovarian hemangiomas, 2; bilateral Krukenberg tumors, 1; mesotheliomas, 1; adenocarcinoma of the appendix, 1; adenocarcinoma of the sigmoid colon, 1.

Record of the state of the endometrium in each case in this study was not made because it has only been recently that accurate criteria in regard to hyperplasia have been accepted. However, in the past four years the endometriums from all uterine specimens have been studied and recorded according to the definitions of hyperplasia of Cullen,<sup>26</sup> and Novak and Martzloff.<sup>25</sup>

A comparison has been made in regard to the endometrial findings in 100 fibromyomatous uteri and in 100 nonfibromyomatous uteri of recent date.

In these 200 cases 20 per cent of the white fibromyomatous uteri and 10 per cent of the Negro fibromyomatous uteri had hyperplasia of the endometrium. Of the nonfibromyomatous uteri removed for chronic salpingitis or for bleeding late in the reproductive life associated with chronic cervicitis, etc., about 15 per cent of the white patients and 20 per cent of the Negro patients had hyperplasia. This quite definitely indicates that there is no special association of endometrial hyperplasia with fibromyomas. This is in agreement with the findings of Brewer and Jones<sup>10</sup> in a study of 100 patients with fibromyomas, in which they found that ovulation, corpus luteum development, and endometrial response were identical to that found in women without fibromyomas. If this then is true, it deletes one of the important arguments in favor of hyperestrinism as the sole etiologic factor in fibromyomas. The studies of Witherspoon, Nelson, Lipschutz and Vargos, and others, quite distinctly indict the female sex hormone as the etiologic factor, but are not convincing as to the exact mechanism. It may be that there is a lowered threshold to stimulation to growth in the isolated affected tissues brought on by trauma of menstruation, pregnancy and labor, or of infection.

We hazard the opinion also that the factor may be an altered hormone, probably estrogenic, the aberration being produced by the influence of other hormones as progesterone, or pituitary hormones or by the endometrium or the myometrium. We suggest experiments in which the experimental animals with normal and with traumatized uteri are injected with serum and urine fractions from fibromyomatous patients to attempt production of true intrauterine fibromyomas rather than intra-abdominal fibrous tumors as are produced by estrogenic hormones.

#### SUMMARY

1. The incidence of fibromyomas in Negro women residing in the neighborhood of Augusta, Georgia, is three and one-third times that of white women.

2. Sixty per cent of white women had tumors smaller than 5 cm. in diameter. Sixty-six per cent of the Negro women had tumors larger than 5 cm. in diameter.

3. Chronic salpingitis was found in one-sixth of the white and more than one-half of the Negro patients with fibromyoma. On the other hand, 40 per cent of all operations for chronic salpingitis revealed complicating fibromyomas.

4. Necrosis in general was about twice as frequent in the tumors of the Negro women as in those of the white women.

5. Fibromyomas were found to be relatively free from malignant complications, but sarcomas were more frequent in the Negro, while carcinomas were more common in the white women.

6. Complicating ovarian changes revealed follicular and corpus luteum cysts to be relatively frequent, cystadenoma to be present in 2 per cent of all fibromyomas, and dermoid cysts in 1 per cent of the white and in 2 per cent of the Negro patients.

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## ECLAMPSIA AND OVARIAN PREGNANCY\*

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A CAREFUL search of the various medical indices failed to reveal a similar case. Only six instances of extrauterine pregnancy with eclampsia have been reported and these have all been tubal or abdominal pregnancies. The first case was reported by Spiegelberg.<sup>1</sup> The patient was a 32-year-old para iv at term. She had five convulsions before her admission to the clinic. She was edematous, with scanty, dark-colored urine that boiled solid. Fetal heart rate was 128. The cervix was open and pushed to the left. The internal os was closed. The baby was in the R.O.A. position. The patient had three more convulsions after admission. She was given ergot and an attempt was made to introduce a catheter into the uterus. It met with some obstruction and the examining finger brought back a piece of decidual tissue. The patient died two days later and autopsy showed dark bloody fluid in the peritoneal cavity and a beginning peritonitis. The fetus, a male, weighed 3,000 Gm., was entirely within the Fallopian tube which showed some sign of rupturing in one place. The uterus was 12 cm. long.

The second was reported from Maygrier's Clinic in Paris by H. Lafon.<sup>2</sup> The patient was a 27-year-old para iii who early in her pregnancy (July, 1895) had severe abdominal cramps that confined her to bed. In August she had a hemorrhage while in the hospital. In September she had edema of the lower extremities and again entered the hospital where a diagnosis of pregnancy complicated by tumor was made. On February 10 she bled a little and two days later began to have convulsions (18 in all). On February 13 Maygrier made an internal examination and diagnosed the extrauterine pregnancy with living baby. The fits continued and the woman died undelivered. The diagnosis of extrauterine pregnancy was confirmed by post-mortem colpotomy.

The third case was reported from Denmark by Holst<sup>3</sup> (1896), who was called after a young girl had lost consciousness and was having convulsions. He found the uterus to be the size of a six months' pregnancy. The urine contained a quantity of albumin. He made an unsuccessful attempt to induce labor by injecting hot water. The convulsions stopped and the patient improved. Five months later a fluctuating abscess formed which opened into the vagina. Small fetal bones escaped. The abscess also opened into the intestines. The first opening was enlarged and the head and most of the fetal skeleton were evacuated. The fistulas closed quickly and recovery ensued.

Schumann<sup>4</sup> reports the case of a patient, upon whom E. P. Davis operated. The patient was a primipara aged about 30 years. Her pregnancy had proceeded normally until between the seventh and eighth month, when after albuminuria had been present for over a week the patient had several eclamptic convulsions. She recovered from this seizure and, although she had some abdominal pains, labor did not come on. The abdo-

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men became smaller and fetal movements could not be felt. Her general health became improved, but an abdominal tumor remained. Bimanual examination gave the impression usually seen in fibroid tumors of the uterus or abdominal pregnancy with retained fetus. The abdomen was opened and a dead fetus of about eight months was in the abdominal cavity. Its sac was attached to the upper portion of the uterus. The placenta was attached to the right broad ligament. The patient made a good recovery.

The fifth case was reported by E. Allen.<sup>5</sup> The patient was a twenty-one-year-old Negro primigravida. The abdominal pregnancy was diagnosed and, while the patient was awaiting term, she had three convulsions. The baby, delivered by laparotomy, weighed four and one-fourth pounds. It cried lustily but died in eight hours. The mother had a psychosis, discharged some placental tissue through the upper end of the wound, but eventually recovered.

The sixth case was reported by Ewart.<sup>6</sup> The patient, 41 years of age, was in the eighth month of her sixth pregnancy. Her fifth pregnancy sixteen years previously was complicated by edema. She had three convulsions. The presentation was a breech and an external version was attempted. Four days later induction of labor was attempted with bougies but was unsuccessful. A month later laparotomy revealed the true condition, i.e., abdominal pregnancy. The patient died on the third postoperative day. Autopsy showed an internal hemorrhage from the placental side.

Our case is, so far as we can find, the seventh extrauterine pregnancy to be complicated by eclampsia. Furthermore, it is the only ovarian pregnancy that has been reported with such a complication.

Mrs. D. A. W., aged 30 years, pregnant for the first time, was due on May 12, 1940. The patient was an only child. Her family history was negative. The patient had scarlet fever at thirteen years. Except for an occasional attack of "flu" there had been no other illness. She was married in 1936. Menses began at eleven, occurred every 26 to 28 days, and lasted five days. She had leg ache sometimes when she menstruated and a leucorrhea of some years' standing. In May, 1939, she flooded two weeks after a regular period, passed clots, and had some cramps. One of us saw her at this time and considered it a functional bleeding. The patient menstruated last on August 5, the flow lasting two days. From September 9 until some time in November the patient had a little bloody vaginal discharge which was never as much as an ordinary menstruation. She was a little nauseated and had canker sores in the mouth. Pelvic examination showed what was thought to be an enlarged retroverted uterus. No lateral masses were palpated and the examination elicited no pain or discomfort. The Friedman test was positive. On December 1, her face and hands began to swell and she had an attack of severe abdominal pain which was relieved by morphine. This was the only attack of severe pain. There was some dysuria before Christmas and, when on her feet, she experienced some lower abdominal discomfort. On January 23 she had three convulsions and was "out," as the patient expressed it, for six days. At this time she was taken to the hospital. Her blood pressure was 210/120 and the urine was loaded with albumin. The treatment consisted of magnesium sulfate by mouth and once by vein, and sodium amytal.

Except for dimness of vision the patient recovered completely from the toxemia. The blood pressure became normal and the albumin disappeared from the urine. Her highest temperature was 101.2° F. on January 25. At that time her pulse was 132. Since then her temperature has been normal. Four attempts were made to induce labor. Each time she had a few cramps when the packing was removed. At the third attempt, Feb. 12, 1940, some material was removed which the pathologist reported to be placental tissue with decidual cells and columnar epithelium. However, no villi were seen. The patient had quite a hemorrhage at this time and a small transfusion was given. At this time some doubt arose as to whether the fetus was within the uterus. A Friedman test was repeated and a soft tissue x-ray was taken in hopes of demonstrating the uterus. The Friedman test was negative and the x-ray showed a small fetal skeleton lying transversely just above the

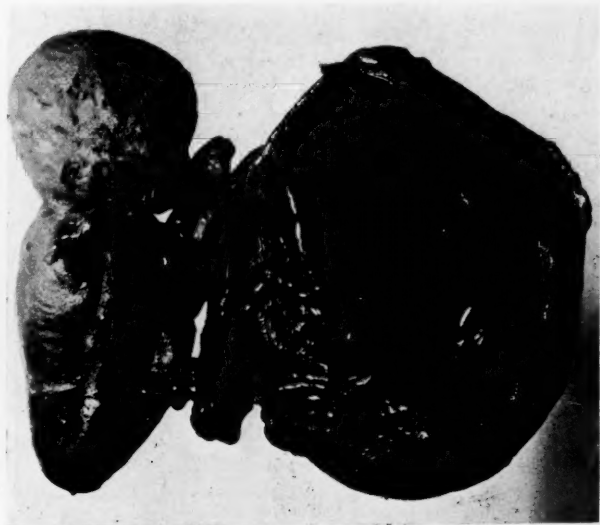


Fig. 1.—Gestation sac opened, showing inside surface of sac and entire fetus.

pubes. No uterine shadow could be seen. The patient was in excellent condition except that she could not read. When she walked about there was a small amount of uterine bleeding. Urine was negative. Blood count was red cells 3,460,000; leucocytes, 13,500; polymorphonuclears, 77 per cent; hemoglobin, 70 per cent; blood pressure, 120/86. Heart and breath sounds were normal. The abdomen was rounded and there was a mass that reached halfway to the umbilicus. Vaginal examination showed marked pigmentation of the mucosa. There was no vaginal discharge. The introitus was nulliparous. The cervix was just back of the pubis. It was soft, uneffaced, and admitted a finger for about an inch. The pelvis was filled with a firm unmovable mass. Examination caused the patient no pain. The abdominal mass could not be outlined by bimanual examination, but seemed to extend about halfway to the umbilicus.

The discussion of the case centered about the question as to whether the fetus was within or without the uterus. The negative Friedman

test indicated that the placenta had ceased to function and, therefore, there was no question but that the fetus was dead. The fact that the uterus did not empty itself and could not be made to empty itself, was the only indication of an extrauterine pregnancy. The contracted uterine body was not visualized on the soft tissue plate. Tissue which had been removed from within the uterus was reported as placental tissue by the pathologist, but this was not conclusive because no villi were found. The presence of decidual cells, according to Telinde, is not absolute proof that pregnancy exists. We finally agreed on the therapeutic test of giving the patient estrin for five or six days. If the dead fetus lay within the uterus, the estrin would in all probability activate the uterus, especially as the placenta had been shown to be inactive. If the estrin failed, a laparotomy should be done.

An abdominal operation was performed April 13, 1940. The uterus was found to be slightly enlarged, flattened, and resting on top of a large mass, which measured 15 by  $9\frac{1}{4}$  by  $8\frac{3}{4}$  cm. The mass was symmetrical and semisolid. It occupied the cul-de-sac and extended to the umbilicus. No free blood was present in the abdominal cavity. The left tube and ovary were normal. In one place there was a small, thinned-out, discolored area in the gestation wall. This condition was caused, no doubt, by the accidental rupture of the uterine wall and the gestation sac by the sound on Feb. 12, 1940. The mass, attached to the right side of the uterus by a long pedicle, was easily freed by blunt dissection and brought up into the wound. Had one not known that a pregnancy existed, he would have thought this to be an ovarian tumor or cyst on a long pedicle. The right uteroovarian ligament was identified, and the right tube appeared normal, except at the distal end, where it was adherent to the mass. The right ovary could not be seen. Large blood vessels were present in the pedicle, which extended from the uterus to the mass, and were the only source from which the gestation sac received its blood supply. The vessels were ligated and the sac was removed after division of the pedicle. The recovery was uneventful. The patient was discharged from the hospital on May 3, 1940.

#### MICROSCOPIC STUDIES

We are indebted to Drs. C. C. Fenton and G. S. Dodds of the University of West Virginia for the following description of the specimen: "Four samples from different regions of the sac showed the following microscopic structure: The greater portion of the thickness of the wall from the inner surface was of necrotic tissue with much blood. Here and there a necrotic villus was seen. The outermost layer of the wall (1 mm. and less in thickness) was not necrotic and showed definite ovarian structure. The stroma was of connective tissue, well vascularized, and rich in spindle-shaped cells, a histologic picture strongly suggestive of the ovary. Definitely diagnostic were scattered ovarian follicles in various stages of growth, from those of small size to large ones with structure like the usual Graafian follicles (Figs. 2 and 3). All of the larger follicles were greatly flattened in a position parallel to the surface of the sac, as would be expected when the ovary had undergone great distention. (Fig. 2 shows a portion of a follicle which measured 4,000 by 70 microns.)"

"The larger follicles were undergoing atresia, as shown by degeneration of the granulosa cells and by the presence of polygonal theca lutein cells among the spindle-shaped cells of the theca folliculi (Figs. 2 and 3).



No germinal epithelium was observed at any of the places sampled, but at one place a mesothelial covering was seen.

"Sections from the wall in the placental area showed many chorionic villi. The superficial zone in these sections was somewhat suggestive of ovarian stroma, but not conclusively so. One probable ovarian follicle of moderate size was seen. On the whole the microscopic studies are sufficient to demonstrate that ovarian tissue was present in the outer stratum of the sac at the several places sampled." Thus the case fulfills all the essential criteria for ovarian pregnancy, viz., (1) the gestational sac occupied the position of the ovary; (2) the tube on the affected side

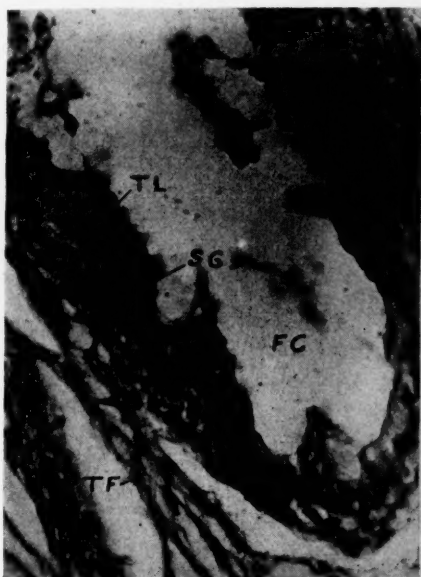


Fig. 2.

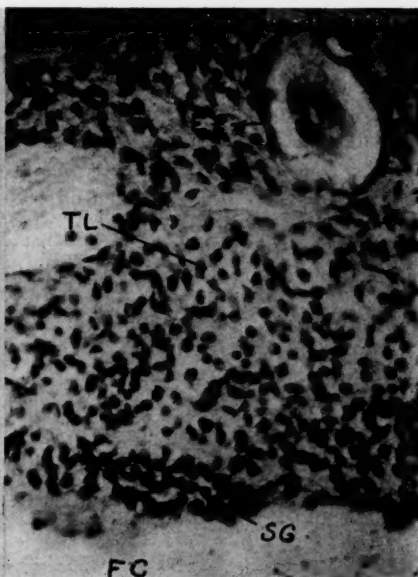


Fig. 3.

Fig. 2.—Part of large ovarian follicle; *FC*, follicular cavity; *SG*, stratum granulosum; *TF*, theca folliculi; *TL*, theca lutein cells. (Photomicrograph under high power.)

Fig. 3.—Shows wall of large ovarian follicle and adjacent ovarian stroma including many theca lutein cells and an early follicle (*EF*). (Photomicrograph under high power.)

was intact and showed no evidence of gestation; (3) the gestational sac was connected with the uterus by the uteroovarian ligament; (4) definite ovarian tissue was found in the wall of the sac in different places; and, (5) there was placental tissue within the ovarian stroma.

#### DISCUSSION

The rarity of the combination of eclampsia and ovarian pregnancy is not surprising. In the first place, eclampsia seldom occurs in the first half of pregnancy. Stander<sup>8</sup> says that fewer than 60 cases have been reported. In the second place, ovarian pregnancy is rare and such a pregnancy rarely extends into the second half of pregnancy. The same can be said for extrauterine pregnancy as a group.

We know that the presence of the fetus is not necessary in order to have eclampsia but that the presence of the placenta is necessary. It



would seem that nature is performing an experiment for us to see if the location of the placenta made any difference. In Spiegelberg's case the placenta was within the tube. In our case it was within the ovary. In Allen, Schumann, and Ewart's it was in the abdominal cavity and presumably that was true also in Holst's and Lafon-Maygrier's cases. Eclampsia is possible, regardless of where the placenta is located. The next question is the relative frequency of eclampsia when the placenta is implanted in or on tissues outside the uterus. The frequency of eclampsia is variously stated as once in 300 to 500 cases. If the same frequency obtained for ectopic pregnancy, it would mean that there have been from 2,100 to 3,500 cases of misplaced gestation of at least five months' duration. Certainly that many have not been reported.

Clinically this group of 7 extrauterine pregnancies with eclampsia is interesting. Most of the patients complained of the usual symptoms of ectopic gestation, i.e., abdominal pains and vaginal bleeding. The toxemia appeared rather earlier than is usual in uterine pregnancy, only one of the patients being at term. The diagnosis of the ectopic pregnancy was made only once before the convulsions occurred. In this case the baby lived for several hours after it was delivered by laparotomy. In 5 cases the babies died before a correct diagnosis was arrived at. In the second case the correct diagnosis was made while the baby was alive, but the mother died undelivered. In the third case the fetal bones were discharged through a fistulous opening. In the fourth, fifth, sixth, and seventh cases, the fetuses were removed by laparotomy and the induction of labor was attempted in the first, third, sixth, and seventh cases. Three mothers died, two undelivered, and the third of internal hemorrhage after operation. Two recovered after stormy convalescences, and two after uncomplicated convalescences. In our case a diagnosis of extrauterine pregnancy was made before operation. That it was a primary ovarian pregnancy was not suspected until the abdomen was opened. Fortunately, she made an uneventful recovery.

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## PUERPERAL UTERINE CONTRACTIONS\*

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**C**ONTRACTIONS of the puerperal uterus are clinically important for two reasons: First and most important, the contractions of the myometrium are necessary for the prevention of hemorrhage; second, they have some interest in relation to after-pains. Immediately after the delivery of the placenta the open sinuses at the placental site are closed by this mechanism. Interlacing fibers of the myometrium act as an efficient means of controlling hemorrhage only when the muscle fibers contract. The physiologic mechanism operating to produce these rhythmic contractions in the post-partum period is not well understood. The pattern of diminishing uterine motility and diminishing response to oxytocics in the puerperium has been shown for the first time by this study. This study has also demonstrated the importance of one factor, estrogenic hormone stimulation, the presence of which is necessary for normal uterine contractions and normal oxytocic response in the puerperium.

### TECHNICAL PROCEDURE

Six normal primiparas have been studied after spontaneous labor at term and low forceps delivery. These patients received no amnesic or analgesic drug during labor, and they were delivered under novocain infiltration and pudendal nerve block. This was done in order to eliminate extrinsic factors which might interfere with the normal physiology of the puerperal uterus. In order to be absolutely certain that no external agent was introduced to confuse the results, epinephrine was not added to the novocain solution. The placenta was allowed to separate spontaneously in each case and was delivered by traction on the cord with the uterus held high in the abdomen. Immediately after delivery of the placenta the patient was redraped, the vagina thoroughly cleaned with tincture of metaphen through a large sterile speculum, the cervix exposed, and a rubber balloon of 100 c.c. capacity introduced by means of a uterine dressing forceps into the fundus. The balloon was attached to a cannula which connected by way of a rubber tube to the mechanical inkwriter. The mechanical inkwriter was so situated that contractions of the uterus were recorded on a revolving kymograph equipped with a timer. The balloon was then inflated with sterile water until pressure in the system was approximately 80 mm. of mercury. The capacity of the uterine cavity immediately after the third stage is 70 to 100 c.c. This capacity diminishes during the puerperium until on the fifteenth day the average capacity is 10 to 25 c.c. There was considerable difficulty in the first experiments because the uterus repeatedly expelled the balloon. This annoying dilemma was finally solved by using a toy

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balloon of the "Micky Mouse" variety with two ears, which when distended with water fixed themselves in the cornua of the uterus, thereby preventing the expulsion of the balloon. Tracings of uterine contractions were recorded immediately after the third stage of labor and on the fifth, tenth, and fifteenth days of the puerperium. After the normal contractions had been recorded, the patient was given 1 c.c. of obstetric pituitrin subcutaneously and a subsequent tracing was obtained. Two of the patients received a course of estrin therapy after the fifteenth day and the effect of this hormone on the puerperal uterus has been observed.

#### NORMAL PUERPERAL CONTRACTIONS

Examination of the tracings will reveal that the contractions were similar in all 6 cases (Fig. 1). It may therefore be assumed that these tracings represent an accurate picture of uterine motility in the puerperium. Contractions which followed the delivery of the placenta were high in amplitude, recurred on an average of every three minutes, and

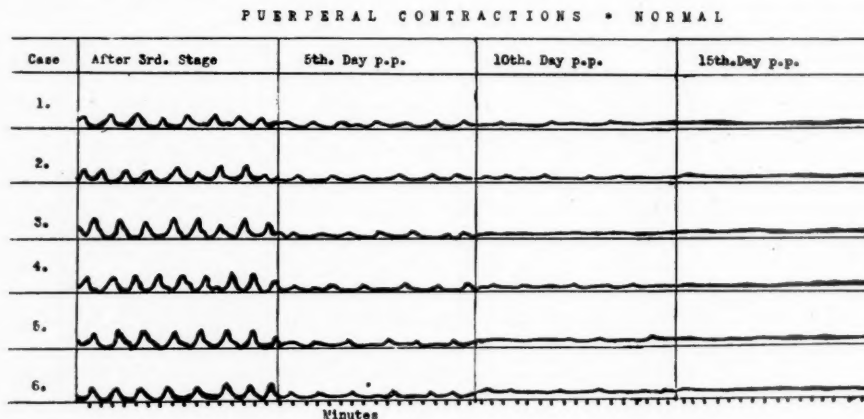


Fig. 1.—Contractions immediately after the third stage are high in amplitude, frequent, and have a long duration. On the fifth day they are greatly reduced in amplitude, rate, and duration. On the tenth day the uterus has lost most of its intrinsic motility and on the fifteenth day the uterus does not contract.

lasted about seventy seconds. On the fifth day the contractions were considerably reduced in amplitude; occurred somewhat more irregularly, every four to seven minutes; and had a much shorter duration, usually lasting thirty seconds or less. On the tenth day uterine motility was practically lost in all cases, there were no regular contractions, and the uteri were atonic. On the fifteenth day of the puerperium the uteri were absolutely nonmotile, contractions could not be elicited by increasing the pressure within the balloon nor by vigorous massage of the fundi.

It is interesting to recall that during pregnancy the estrogenic hormone is produced in an ever increasing amount until shortly before or at the onset of labor. The urinary titers of this hormone fall off abruptly after the delivery of the placenta. This would be expected in view of the fact that the placenta is by far the most efficient organ of estrin production. Woman is more nearly castrate in the midpuerperium, endocrinologically speaking, than at any other time during her reproductive life. This has been shown by studies on urinary estrin titers and biopsies of the vaginal epithelium. The progressively diminishing

uterine motility during the puerperium parallels the decline of the estrin titer in the blood, as this hormone is eliminated during the postpartum period. It would certainly seem logical to assume, in view of this observation, that the loss of intrinsic uterine motility as shown in the tracings was the result of the lack of estrin stimulation. This hypothesis, it is thought, may be strengthened by studies soon to be made relative to the return of uterine contractions and their relationship to endogenous estrin recovery. It will be shown in this report that intrinsic motility may be restored by the exogenous administration of estradiol benzoate.

#### OXYTICS IN THE PUERPERIUM

The same 6 patients in whom spontaneous contractions have just been described were given 1 c.c. of pituitrin subcutaneously immediately after the previous tracings were recorded. When the tracings were examined, it was noted that the response immediately after the third

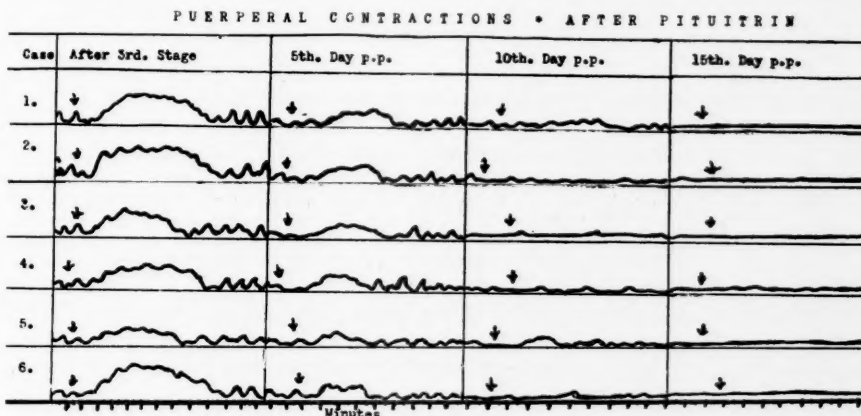


Fig. 2.—Arrows indicate point at which patients received 1 c.c. of pituitrin s.c. Note the marked oxytocic response immediately after the third stage, less response on the fifth day, no response in 4 patients and only slight response in 2 patients on the tenth day, and no response in any patient on the fifteenth day.

stage was marked. The uterus became tetanic within three to four minutes, and this tetany persisted for a variable length of time, in most cases about seven minutes. Perhaps even more significant than the tetany was the stimulation to more frequent contractions of a higher amplitude which followed the tetany. This secondary response was a most variable one, lasting in 1 case ten minutes and in another, over sixty minutes. On the fifth day the oxytocic response to pituitrin was reduced. There was moderate tetany followed by a period of hypermotility which lasted for a variable length of time. On the tenth day post partum, there was a very slight response to pituitrin in two cases followed by some motility but such response was absent in 4 cases. All of the cases failed to show any response on the fifteenth day. The uterus in the late puerperium loses its intrinsic motility and its ability to react to pituitrin (Fig. 2).

#### EFFECT OF ESTRADIOL BENZOATE

It may be assumed that the loss of uterine motility in the puerperium is the result of estrin depletion. The loss of uterine sensitivity parallels

the fall in blood estrin. Two patients (Cases 4 and 5) were given 1 mg. of estradiol benzoate (progynon B) daily on the fifteenth, sixteenth, seventeenth, and eighteenth days of the puerperium. Tracings taken on the eighteenth day show a good return of spontaneous contractions of the uterus (Fig. 3). The contractions are low in amplitude, occur every two to three minutes, and have a relatively short duration. The most significant recovery which resulted from the estrin therapy was demonstrated by the marked response to pituitrin which followed the estrin as compared with the total absence of response in the nontreated cases (Fig. 2). This observation is of real practical importance in relation to hemorrhage during the late puerperium. It would certainly seem wise in the light of these results to treat all hemorrhage after the fifth day post partum by first priming the uterus with estradiol and administering the oxytocic after the uterus has been resensitized. The administration of oxytocics is worthless after the tenth day. How long a time is required

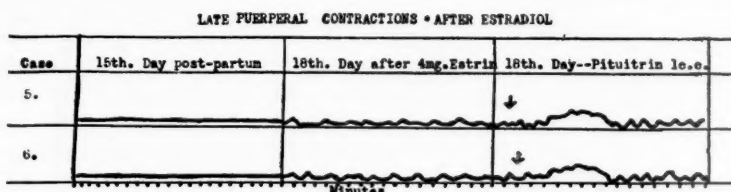


Fig. 3.—Uterus is quiet on the fifteenth day post partum; no intrinsic motility. After 1 mg. of estradiol benzoate for four days, intrinsic motility is restored and the uterus again becomes sensitive to pituitrin.

to resensitize a uterus with estrin in the late puerperium, I do not know but I fear that, with the natural estrogens, a minimum of twenty-four hours is required. In my experiments I arbitrarily took the tracing after four days of therapy. Perhaps diethylstilbestrol may act more quickly.

#### CONCLUSIONS

1. Puerperal uterine contractions have been studied by means of an intrauterine balloon connected to a mechanical inkwriter which records the tracings of the contractions upon a revolving kymograph equipped with a timer.
2. The uterus rapidly loses its spontaneous contractions during the puerperium. After the tenth day no contractions occur. This loss parallels the drop in blood estrins.
3. Oxytocic response to pituitrin is rapidly lost during the puerperium. After the tenth day no response can be recorded.
4. A certain degree of intrinsic motility can be restored by the administration of estrin and the uterus is again sensitized to pituitrin. Puerperal hemorrhage after the fifth day should always be treated by estrin plus pituitrin.

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## COMPARATIVE MEASUREMENTS OF THE FEMALE PELVIS\*

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**T**HERE are four methods by which the diameters of the pelvis may be measured: (1) The diagonal conjugate may be obtained and the true conjugate estimated from it by subtracting 1.5 to 2 cm., (2) X-rays may be directed into the pelvic inlet by the technique of Thoms, Torpin, and others, (3) X-rays may be directed lateral to the pelvic inlet by the technique of Thoms, Jacobs and others, and finally, (4) the patient may be operated upon and the true conjugate measured directly.

Classification of the architecture of the pelvis is possible by the use of the x-ray. Several classifications are available. The more recent stem from the work of Turner and are based on morphology. Caldwell, Moloy, and Thoms have led in this work. They have borrowed extensively from the anthropologist, basing their classification on the contour of the pelvic inlet.

This study is undertaken with the purpose of comparing the antero-posterior diameters of the pelvis obtained by the four methods outlined above. Such a comparison should assist us in evaluating the meaning of the diagonal conjugate; it should further assist us in formulating an opinion as to the accuracy of x-ray pelvimetry. Furthermore, if in addition to diameters, the structure and contours of the birth canal are studied both by x-ray and physical means, we are aided in the clinical evaluation of the female pelvis.

### PELVIC CLASSIFICATION

#### CALDWELL AND MOLOY

Gynecoid  
Android  
Anthropoid  
Platypelloid  
Mixed forms  
Asymmetrical

#### THOMS

Mesatipellic  
Brachypellic  
Dolichopellic  
Platypellic  
Mixed forms  
Asymmetrical

The classification used is that of Caldwell and Moloy. The classification of Thoms is included for the purpose of clarity and comparison. It should be noted that Thoms uses the terms mesatipellic (round inlet) and brachypellic (transversely oval inlet) to describe Caldwell and Moloy's gynecoid pelvis. In the Thoms' system, the dolichopellic pelvis is the anthropoid pelvis of Caldwell and Moloy; the platypellic pelvis is obviously the same as the platypelloid pelvis. Thoms does not include

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Caldwell and Moloy's android pelvis in his classification, holding that this is not a true parent type, but represents an abnormal pelvis showing the effect of obscure growth or nutritional defects.

*Gynecoid.*—The pelvic inlet is circular or slightly flattened anteroposteriorly; its greatest transverse diameter passes through the central part of the anteroposterior diameter. There is a wide sacrosciatic notch, broad at the base and at the apex. The sacrum is backward in direction with a deep concavity. There is a wide subpubic angle and the pubic rami are short, giving a decreased depth to the pelvis.

*Android.*—The pelvic inlet is "heart shaped" so that the forepelvis is narrowed and the available space is diminished. The available space in the posterior pelvis is encroached upon by the exaggerated promontory. The greatest transverse diameter of the inlet is displaced posteriorly. The bore of the pelvis converges toward the outlet, the "funnel pelvis." The sacrosciatic notch is narrow at the apex, indicating a decreased bone length in the posterior iliac portion of the inlet. The sacrum is usually forward with a poor concavity. The subpubic angle is narrow and the pubic rami are lengthened giving an increased depth to the pelvis.

*Anthropoid.*—The inlet is relatively long anteroposteriorly and short transversely. The greatest transverse diameter is at the midpoint of the anteroposterior diameter. The direction of the sacrum is usually backward with a marked promontory and a shallow concavity. There may be moderate narrowing of the subpubic angle.

*Platypelloid.*—The anteroposterior diameter of the inlet is relatively shortened and the transverse diameter relatively widened. According to Thoms there must be a difference of 3 cm. or more to be so classified. The sacrosciatic notch appears narrowed; there is usually a wide subpubic angle.

#### . TECHNIQUE

The technique of obtaining the anteroposterior diameter of the pelvic inlet by the four available methods requires further consideration: First, *the diagonal conjugate and the estimated true conjugate*. The details of obtaining this measurement require no explanation. It is customary to subtract 1.5 to 2 cm. from the diagonal conjugate to estimate the conjugata vera. Second, *the anteroposterior diameter of the pelvic inlet at operation*. At the time of abdominal operation, this diameter may be measured directly. The DeLee outlet pelvimeter is particularly suited for this purpose. The operator holds one arm of the pelvimeter against the promontory of the sacrum; his assistant places the other arm against the inner surface of the symphysis 1.5 cm. inferior to the superior margin. A reading is taken and recorded. For the purpose of eliminating the personal factor so far as possible, the operator and the assistant may reverse the manner in which the measurement is made and another reading recorded. Third, *the anteroposterior diameter* by means of x-rays directed perpendicular to the plane of the pelvic inlet.

The method is that of Thoms as modified by Torpin for speed and convenience. The patient is seated on the apparatus and the posterior marker set at the junction of the fourth and fifth lumbar vertebrae; the anterior marker is set at a point 1.5 cm. inferior to the superior margin of the symphysis. The patient is adjusted so that the two

markers are equal, since Caldwell has shown that a distortion of contour of the inlet may occur if the plane of the pelvic inlet is not at right angles to the center ray. An exposure is made according to the body structure and degree of pregnancy of the woman, and she is removed from the apparatus without disturbing the x-ray tube, markers, or plate. A lead grid perforated at centimeter intervals is placed on the markers and a flash exposure made. Fourth, *the anteroposterior diameter by means of x-rays directed lateral to the pelvic inlet.*

The method is that of Thoms and Jacobs modified by ourselves for speed and convenience. The patient stands with the right hip against the vertical table top, the left hip is directed toward the x-ray tube. She is adjusted so that she is at exact right angles to the center ray. The center ray is directed at a point 3 cm. below the anterosuperior iliac spine and at the center of the hip. An exposure is made according to the body structure and the degree of pregnancy. Before leaving this position the distance from the genital crease to the table top is measured. The patient is removed, the table is returned to the horizontal and the Torpin apparatus replaced. The markers are set at the distance measured from genital crease to table top minus one-half inch for thickness of the board. The lead grid is placed upon them and a flash exposure is made.

It is seen that by the use of the x-ray, two flat plates of the pelvis are obtained. The first, an anteroposterior picture, reveals the contour of the pelvic inlet; in addition to this a centimeter scale has been superimposed, permitting the reading of the diameters of the inlet. These diameters are read directly from the plate since the lead grid has been placed in the plane of the inlet and any distortion due to the x-ray is reproduced in equal amount in the centimeter markings on the plate.

The second, a lateral picture, reveals the architecture of the birth canal. From it the position, shape, and concavity of the sacrum, the contour of the sacrosciatic notch, and the depth of the pelvis may be seen. In addition, a corrected centimeter scale has been superimposed in the sagittal plane of the pelvis. The anteroposterior diameter of the pelvic inlet may be read from the grid markings (although not directly). An individual scale is made for each lateral plate, this applied to the film and the reading taken.

#### COMPARATIVE MEASUREMENTS AND CLASSIFICATION

In this study first, the anteroposterior diameter of one x-ray technique is checked for accuracy against the same diameter obtained by the second x-ray technique. Second, the anteroposterior diameter of the pelvis obtained by x-ray is checked for accuracy against the same diameter measured at the time of operation. Third, the anteroposterior diameter obtained by x-ray is compared with the diagonal conjugate. Fourth, the anteroposterior diameter measured at the time of operation is compared with the diagonal conjugate.

From a study of Table I it is seen that in 83 per cent of the cases the anteroposterior x-ray compared favorably with the lateral x-ray. The anteroposterior diameter was the same in both, allowing an error of 4 mm. This error seems acceptable since in our experience the same observer will not re-measure a diameter closer than that figure. Furthermore, two observers measuring the same diameter will vary as much as 4 mm. in their readings.

TABLE IA. SUMMARY OF STUDY

PROCEDURE	NO. CASES
Studied by x-ray pelvimetry	300
Studied with both anteroposterior and lateral plates	229
No difference in true conjugate comparing antero-posterior and lateral x-ray plates	191 (83%)
Studied digitally (diagonal conjugate)	222
Measured at time of abdominal operation	44

TABLE IB.

VARIATIONS IN GROUP	CM.
Average difference in true conjugate comparing anteroposterior and lateral x-ray plates	0.34
Shortest anteroposterior x-ray diameter	8.75
Longest anteroposterior x-ray diameter	14.0
Shortest x-ray transverse diameter	10.5
Longest x-ray transverse diameter	15.0
Longest diagonal conjugate	13.0
Shortest diagonal conjugate	9.0
Longest operative measurement	13.0
Shortest operative measurement	8.0

It must be assumed that the most accurate method of measuring the anteroposterior diameter of the pelvis is the one actually made under direct vision at the time of abdominal operation. Comparison of these measurements with those made by x-ray should give an indication of the accuracy of the latter as a measuring device. As indicated in Table II, in 40 per cent of the cases measured by the first x-ray technique and in 41 per cent of the cases measured by the second x-ray technique, the operative and x-ray measurements were the same. This is not a high degree of accuracy. Dismissing for the purpose of discussion the errors due to faulty technique, the disagreement in the remaining 60 per cent of the cases may be explained on this basis; that the x-ray measures bone-to-bone only and any other technique, including the measurements made at the time of operation, is soft tissue-to-soft tissue measurement. We were frequently surprised at the amount of tissue lying on the inner

TABLE II. COMPARISON OPERATIVE MEASUREMENTS WITH ANTEROPOSTERIOR AND LATERAL X-RAY MEASUREMENTS IN 44 CASES

A-P x-ray longer by	0 (equal)	0.5-0.9 cm.	1.0-1.4 cm.	1.5-1.9 cm.	TOTAL
Number of cases	18 (40%)	9	4	3	34
A-P x-ray shorter by	0 cm.	0.5-0.9 cm.	1.0-1.4 cm.	1.5-1.9 cm.	
Number of cases		5	4	1	10
Lat. x-ray longer by	0 (equal)	0.5-0.9 cm.	1.0-1.4 cm.	1.5-1.9	
Number of cases	17 (41%)	15	5	2	39
Lat. x-ray shorter by	0 cm.	0.5-0.9 cm.	1.0-1.4 cm.	1.5-1.9 cm.	
Number of cases			2		2

surface of the symphysis. In support of this explanation is the further factor, seen in the table, that in the majority of these cases the x-ray measurement was longer than the corresponding measurement made at operation.

One is accustomed to subtract 1.5 to 2 cm. from the diagonal conjugate to obtain the true conjugate. A measurement so obtained is obviously not an accurate one since it is based on estimation. It seemed to us that by comparing the diagonal conjugate with the true conjugate, measured by x-ray and at the time of abdominal operation, some opinion as to the clinical value of this estimated true conjugate might be forthcoming.

TABLE III. COMPARISON DIAGONAL CONJUGATE WITH ANTEROPOSTERIOR AND LATERAL X-RAY MEASUREMENTS IN 222 CASES

A-P x-ray longer by	0 (equal)	0.5-0.9 cm.	1.0-1.4 cm.	1.5-1.9 cm.	2 plus cm.	TOTAL
Number of cases	89 (40%)	58 (26%)	0	0	0	147
A-P x-ray shorter by	0 cm.	0.5-0.9 cm.	1.0-1.4 cm.	1.5-1.9 cm.	2 plus cm.	
Number of cases	0	43 (14%)	0	28	4	75
Lat. x-ray longer by	0 (equal)	0.5-0.9 cm.	1.0-1.4 cm.	1.5-1.9 cm.	2 plus cm.	
Number of cases	64	59	0	0	0	123
Lat. x-ray shorter by	0 cm.	0.5-0.9 cm.	1.0-1.9 cm.			
Number of cases	0	32	22			54

Attention is called to three facts in Table III comparing the diagonal conjugate and the x-ray true conjugate: (1) The fact that in 40 per cent of the cases the diagonal conjugate and the x-ray true conjugate were the same; (2) the fact that in 14 per cent of the cases the diagonal conjugate was greater than the x-ray true conjugate as would be anticipated, but that contrary to expectation this difference is neither 1.5 cm. nor 2 cm., but is less than 1 cm.; (3) the fact that in 26 per cent of the cases so compared the diagonal conjugate was actually less than the true conjugate. In this last group of cases, subtracting 1.5 to 2 cm. from the diagonal conjugate would not only fail to approximate the true conjugate, but would greatly increase the error already present in any estimated measurement.

So far as the clinical evaluation of the pelvis is concerned one would, therefore, seem nearer correct in 80 per cent of these cases if the unmodified diagonal conjugate were accepted as the same as the x-ray true conjugate. In this group of cases one would have been right in only 12 per cent of the cases if 1.5 cm. were subtracted from the diagonal conjugate; and right 4 times out of 222 if 2 cm. had been subtracted.

Similar conclusions are apparent when the diagonal conjugate is compared with the true conjugate measured at the time of abdominal operation (Table IV). Here the following facts, closely corresponding to the above, are found: (1) that in 32 per cent of the cases the diagonal conjugate measured digitally and the true conjugate measured at the time of operation are the same, (2) that in 27 per cent the diagonal conjugate is greater but by less than 1 cm., and (3) that in 18 per cent the diagonal conjugate was less than the true conjugate.



TABLE IV. COMPARISON DIAGONAL CONJUGATE WITH THE OPERATIVE MEASUREMENT IN 44 CASES

Diag. Conj. greater by	0 (equal)	0.5-0.9 cm.	1.0-1.9 cm.	2 plus cm.	TOTAL
Number of cases	14 (32%)	12 (27%)	8	2	36
Diag. Conj. less by	0 cm.	0.5-2 plus cm.			
Number of cases	0	8 (18%)			8

It is, therefore, seen that in this group the same conclusions are suggested: First, that in 77 per cent of the cases one is nearer correct in the clinical evaluation of the pelvis if the unmodified diagonal conjugate is accepted as the same as the true conjugate; second, that if 1.5 cm. were subtracted, one would have been right so far as the estimated true conjugate is concerned in 18 per cent of these cases only; third, that if 2 cm. were subtracted, one would have been right twice out of 44 times.

TABLE V. COMPARISON OF AVERAGES

AVERAGE DIAMETER ENTIRE GROUP	CM.
Anteroposterior x-ray	11.5
Transverse x-ray	12.6
Diagonal conjugate	11.5
Anteroposterior operative	11.2

Upon inspection of Table V, it is interesting to note that the same conclusions as those just outlined are indicated when one considers averages rather than actual diameters. It is seen that the average anteroposterior diameter by x-ray, the average true conjugate by actual measurement, and the average diagonal conjugate for this group are essentially the same measurement.

TABLE VI. CLASSIFICATION OF PELVES

CLASSIFICATION AFTER CALDWELL AND MOLOY	NO. CASES	PER CENT
Gynecoid	222	74.0
Android	4	1.33
Anthropoid	5	1.66
Platypelloid	5	1.66
Mixed forms	58	19.0
Asymmetrical forms	5	1.66

The classification (Table VI) of this "average pelvis" for the series is gynecoid. Its inlet would appear round to the eye, but upon actual measurement it would be slightly oval in the transverse direction. Seventy-four per cent of the pelves were gynecoid; 19 per cent were mixed forms. Concerning this latter classification, an explanation is necessary. A pelvis may be classified as mixed (for instance gynecoid-android) by which is meant that the posterior pelvis is gynecoid in structure and the forepelvis in android. In this series a pelvis was not classified as mixed unless the modifying factor was felt to be so marked as to influence the clinical course of labor.

## SUMMARY AND CONCLUSIONS

Since the use of x-ray in obstetrics, four methods are available for studying the anteroposterior diameters of the pelvis. A fair degree of accuracy is possible by x-ray methods; in addition, carefully made plates afford a satisfactory means of classifying the pelvis under study. It is necessary to emphasize, however, that the x-ray is not the answer to an obstetric problem in itself; nor is it an infallible instrument of precision; it is another means of study which when added to the usual pelvimetry, physical examination, laboratory studies, etc., assists us in obtaining the desired answer. When compared with the diagonal conjugate and the true conjugate, measured at the time of operation, it gives us a new insight into the value of the diagonal conjugate. In this series the unmodified diagonal conjugate appeared to be a more accurate measurement in indicating the true conjugate than the one from which 1.5 to 2 cm. has been subtracted. In the series of 300 women studied, the gynecoid pelvis was the predominating type; mixed forms were the next most frequent. The true "parent type" of pelvis is probably less often seen and the mixed forms more often seen than these statistics would indicate. Our qualifications for admission into the latter group may be responsible for this fact.

226 HILLSBORO STREET

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PLACENTAL POLYP WITH SEVERE LATE PUERPERAL HEMORRHAGE\*

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HAGSTROM,<sup>1</sup> in May, 1940, reported a case of severe late puerperal hemorrhage due to placental polyp. He points out that the occurrence of such a condition is apparently infrequent, and bemoans the paucity of reports of such cases, both in obstetric textbooks and in the general literature.

The following case is presented because of its interest from the point of view of dangerous late hemorrhage and even more so because of the difficulty in differential diagnosis which causes the warning for a most careful pathologic examination to be made in any suspicious case.

## CASE REPORT

Mrs. L. R., a 23-year-old, white, gravida ii, para i, was delivered of her second baby at term on Jan. 8, 1941, the prenatal course and labor having been perfectly normal. Labor was of four hours and five minutes' duration. The placenta was delivered by modified Credé maneuver six minutes after the birth of the baby, and was apparently complete and intact. The blood loss was estimated at 150 c.c. The immediate puerperal recovery was uncomplicated except for an acute rhinitis in the

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third and fourth days post partum, and the patient was discharged from the hospital in good condition on Jan. 15, 1941.

On the eighteenth day post partum, the patient telephoned that she was having cramplike uterine pains and also pain in the region of the appendix. When seen at home she exhibited no unusual symptoms except for a moderate tenderness over the uterus and in the area of the right ovary, and a slight increase in the lochia, which had previously almost stopped. She was given a course of ergotrate, and bed rest and heat to ovarian region were advised.

The following day she felt well, and remained so until the twenty-second post-partum day, Jan. 30, 1941, at which time she had a sudden massive hemorrhage, estimated at 1,500 c.c. The patient was immediately returned to the hospital and taken to the operating room within an hour of the hemorrhage. Exploration of the uterine cavity with the gloved finger revealed the entire cavity to be filled with tissue which had a rather firm, leathery feel, and which was densely adherent. Several small pieces of this tissue were removed by the gloved finger, and the diagnosis on frozen section, later by permanent section, was chorion-epithelioma.

At the time of removal of the above tissue, the patient became practically pulseless and in apparent shock. The uterus was quickly packed, and the patient was returned to her room. She responded well to general supportive measures. X-ray examination on Jan. 31, 1941, showed no involvement of the chest.

On Feb. 1, 1941, following a preoperative transfusion of 475 c.c. of citrated blood (the red blood count being 3,040,000 and the Hb 60 per cent prior to transfusion), a panhysterectomy was performed. The postoperative course was uneventful.

Sections from the uterus were diagnosed as syncytioma. Because of this variation in the report on the tissue removed from the uterine cavity, and that adherent in the uterine cavity, the specimen was taken to another pathologist who made independent sections and whose opinion was that the tissue showed no definite malignant changes, but merely obliteration of the uterine wall by pressure.

With this further confusion in the pathologic picture, it was felt advisable to secure still another opinion, principally because of the prognosis for the patient. Therefore, the specimen was sent to the pathology department of one of the nearby university medical schools. They sent a most complete and detailed report, which may be summarized by the following paragraph:

"It is our impression that differential diagnosis in this case rests between syncytial endometritis or placental polyp. It is our impression after review of the gross and microscopic findings that the picture is best described by the term placental polyp and represents retained placental tissue which has maintained its attachment to the uterine wall and with which it is incorporated. This process might be included by some under the first mentioned term, syncytial endometritis, though the lack of syncytial infiltration is against this designation. It is our impression, thus, that we are dealing with a persistence of placental elements with associated infection and necrosis and not with a tumor process."

#### COMMENT

In describing chorionepithelioma, DeLee<sup>2</sup> mentions that one of the many names by which it has been called is "invasive placental polyp."

Undoubtedly the dividing line between polyp and chorionepithelioma is in many cases very finely drawn, and it is the feeling of this author that a panhysterectomy should be immediately performed on such doubtful cases.

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ANENCEPHALUS (WITH ACUTE HYDRAMNIOS)  
DIAGNOSED BY X-RAY\*

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**A**NENCEPHALY is commonly associated with hydramnios. Clinically, this condition is rarely diagnosed before the onset of labor and more rarely before the rupture of the membranes. Roentgenography is a reliable means of demonstrating this anomaly long before it is possible to make the diagnosis by physical examination.

In our private practice, the discovery of two cases of anencephaly during the eighth month of pregnancy stimulated us to review the literature. We were surprised to find that only 31 cases had been reported. Harbeson<sup>1</sup> reviewed the literature in 1938, finding a total of 25 cases, to which he added one of his own. We were able to find 5 other cases, reported about the same time, which were not included in Harbeson's paper. These cases were distributed as follows: (1) Astier and Vernet<sup>2</sup> reported 2 cases in 1937, (2) H. Kuckens<sup>3</sup> 1 case in 1937, (3) Schubert<sup>4</sup> 1 case in 1937, and (4) S. G. Schenck<sup>5</sup> 1 case in 1940.

In all cases reported, where a reason was given for making the x-ray examination, it was one or all of the following: (1) Absence of the fetal head on clinical examination, (2) inability to determine the presentation and position by clinical examination, (3) acute hydramnios suggesting fetal anomaly. The x-ray findings in these cases were quite uniform, showing the absence of the bones of the calvarium and the bones at the base of the skull as an irregular mass, usually quadrangular in shape.

In our first case, x-ray examination was made because of the peculiarly shaped mass presenting in the pelvis, and because the patient had acute hydramnios. In our second case, in the presence of acute hydramnios, we were unable to feel a presenting part.

In reporting these two cases, we call your attention to the marked similarity in history and clinical course.

**CASE 1.**—Mrs. W. B. H., aged 30 years, para 0, gravida iv, had been married nine years. Her general health was good. Three abortions, at approximately two and one-half months, occurred during the past three years. The last menstrual period, Sept. 18, 1939. The expected date of confinement was June 25, 1940. Physical examination was essentially negative. All routine laboratory studies were negative except a basal metabolism rate of -12, and blood cholesterol 229 mg. per 100 c.c. of blood.

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Due to three previous unsuccessful pregnancies, more than average precautions were taken to preserve this one. She was given lipolutin, one unit every five days, until the end of the fifth month, and thyroid extract,  $1\frac{1}{2}$  gr., daily throughout pregnancy.

Her pregnancy was uneventful until May 14, 1940, when the pelvic examination revealed an irregular mass presenting deep in the pelvis. Acute hydramnios was evident. The patient had gained a total of 36 pounds during pregnancy, six pounds during the last three weeks. Her blood pressure and urine had been normal.

*Roentgen Findings.*—Anencephaly with face presentation.

Labor began spontaneously on June 18, and thirteen hours later she was delivered of a dead fetus, presenting all the characteristics of anencephaly.

CASE 2.—Mrs. J. M., aged 32 years, para 0, gravida iii, had been married nine years. Her general health was good. Two spontaneous abortions occurred at three months during the past four years. Smith-Hodge pessary was inserted for temporary relief of a third-degree retroversion of the uterus on April 28, 1939.

Her last menstrual period occurred on Aug. 4, 1939. The expected date of confinement was June 11, 1940. General physical examination was negative. Uterus was held in position by the pessary.

Due to a long period of sterility and two unsuccessful pregnancies, this patient, likewise, was instructed to limit her activities a great deal more than in the average case. She was given corpus luteum, 1 c.c., every three days until the end of the fifth month. She was given thyroid extract, gr.  $\frac{1}{2}$ , twice daily. Her pregnancy was uneventful. She gained a total of 20 pounds. Her blood pressure and urinary findings were always negative. On May 5, she was found to have acute hydramnios. Upon vaginal examination no presenting part could be felt. Roentgen examination, due to the excessive amount of amniotic fluid, did not show the clear-cut detail desired. The presence of anencephaly was demonstrated with that part presenting at the pelvic inlet.

Labor began spontaneously on June 2 and, after twenty-seven hours, the patient was delivered by podalic version and extraction. The fetus, a typical anencephalus, was dead.

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## CHANGES IN THE FEMALE GENITAL TRACT DURING THE PUERPERIUM INDUCED BY SEX HORMONE THERAPY

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THE ease with which modern therapeutists can prescribe constant, effective dosages of both synthetic male and female sex hormones has resulted in an ever-widening scope of clinical uses. Their employment has been most apparent in problems of abnormal uterine bleeding, failure of ovulation, sterility, ante-partum bleeding, or menopausal harassments. Sex hormone therapy in the postpartum phase has been limited to puerperal breast comfort<sup>1</sup> or to efforts to hasten involution of the uterus with resultant improvement in puerperal morbidity.<sup>2</sup>

The extensive literature which already has accumulated regarding the use of the estrogens and of the androgens in puerperal breast problems need not be reviewed. The majority of investigators feel that there is a definite place for such therapy, although the information regarding the side-effects of these agents is but slight. This paper will inquire into those changes.

Markee<sup>3</sup> noted the maintenance of good blood supply to the uterus using the estrogens. Wolf<sup>4</sup> and Falls, Lackner and Krohn<sup>5</sup> reported that the estrogens lend better tone to the post-partum uterus by increasing its contractility, and the former additionally noted that estrogens sensitize the myometrium to oxytocics. With this in mind, Connally and others<sup>2</sup> employed the estrogens in 200 cases in an effort to decrease post-partum morbidity. Five milligrams of diethylstilbestrol were given by mouth, beginning immediately after delivery, and were continued as a 5 mg. daily dose for the first twelve post-partum days. Morbidity (defined as a temperature of 100.4° F. for any two twenty-four-hour periods during the puerperium) was lowered from 12.8 per cent in a control series to 4.0 per cent in the estrogen-treated group. No untoward effects were noted, lochia was unchanged, and the rate of involution studied at twenty-one days post partum was thought to be hastened somewhat.

### MATERIAL AND METHODS

The cases selected for study were ward cases from the Boston Lying-in Hospital. These patients were not allowed to nurse because of still-born infants, previous breast abscess, or maternal disease. One series of 12 patients was given 10 mg. of diethylstilbestrol by mouth daily for the first twelve days post partum, the first dose being given immediately after delivery. A similar series of 12 patients was given 10 mg. of methyl testosterone by mouth, beginning immediately after delivery, and being continued for the first twelve days. For comparison with

these two groups of cases, 12 patients treated with female sex hormone and 12 treated with male sex hormone, a random group of 12 cases was chosen from the post-partum wards to serve as controls.

A generous biopsy specimen was taken from both walls of the uterine cavity of each of these patients, using a suction curette. At the same time, smears were taken from the vaginal epithelium. Only one patient was used to supply these simultaneous endometrial and vaginal specimens for any one day in the post-partum period. In this way, individual variations were minimized and yet a large group of patients could be sampled. One case from each group was followed beyond this twelve-day period, or until regeneration of the uterine mucosa was completed apart from the sex hormone effects (to be described). The cases were without complication and thus represented a good cross-section of the average post-partum patients.

The endometrial specimens were fixed in Bouin's solution and stained with hematoxylin-eosin. The vaginal smears were stained with acid fuchsin.

The dose of either estrogen or androgen was fixed arbitrarily at 10 mg. by mouth daily, for it represented about the average dose recommended for either suppression of lactation or as an aid in hastening involution.

This, then, gave three essentially similar groups of cases of 12 each, with more prolonged study in one case of each of the hormone-treated groups, one case in each group being followed until regeneration was complete. Individual variations are noted in the biopsy specimens, but the average trend remains of significance.

#### PATHOLOGIC DESCRIPTIONS

In a previous study I<sup>6</sup> followed the rate of the regeneration of the uterine mucosa in the normal post-partum patient, and studied the effect of lactation. Briefly, the endometrium was regenerated completely by twelve days post-partum, although the placental site was not cast off until six or seven weeks post partum, as Williams<sup>7</sup> demonstrated. Ovulation took place in the nonlactating post-partum patient on an average of six weeks post partum, with menstruation at eight weeks. Lactation arrested the endometrium in a repaired, resting phase, which persisted until lactation ceased. Occasionally, there would be evidence that the normal ovarian cycle would break through the pituitary inhibition of lactation, and that the patient would ovulate and menstruate while yet lactating; this latter is a well-known clinical fact.

Since this is reported in detail elsewhere,<sup>6</sup> only cursory mention will be made of this normal rate of regeneration as compared to the rate and order of regeneration in patients treated with the synthetic sex hormones as outlined. No significant departure from the usual picture is found in the first two days post partum of the hormone-treated cases, so description of these slides will not be given.

*Female Sex Hormone Influence, Endometrial Biopsies.*—These patients all had been given orally 10 mg. daily of diethylstilbestrol, and each day represents an individual case.

*Three-day post-partum specimen:* Vacuolated decidual cells with no definite evidence of involution, the cell outlines were somewhat indistinct. The gland epithelium was vacuolated with swelling of the

nucleus; the stroma had slight infiltration of acute and chronic inflammatory cells; there was some trophoblast yet present.

*Four-day post-partum specimen:* Slough was present, the decidua was still well preserved as were the glands. The cytoplasm of each was swollen, less vacuolated, and the nuclei of both glandular epithelium and stroma were light staining and swollen. There were yet present some placental site synctiotrophoblastic cells in the myometrium. Rare mitotic figures were seen in the glandular epithelium (they were seen first at this stage in the normal post-partum uterus<sup>6</sup>).

*Five-day post-partum specimen:* Slough was present; there were many mitotic figures present in the glands which were pseudostratified in type. The mitotic figures were in all phases and were much in excess of the normal post-partum five-day endometrium. The decidua still was well preserved, with the nuclei large and clear, looking almost like predecidua.

*Six-day post-partum specimen:* There was superficial necrosis; mitotic figures were marked in the glands with evidence of increased rate of regeneration. The stroma was both predecidual and decidual in type with large clear nuclei.

*Seven-day post-partum specimen:* Regeneration was still present within the glands, although fewer mitoses were seen. The stroma was of indifferent type, but was well maintained. There was some placental site trophoblast left.

*Eight-day post-partum specimen:* The glands were regenerating rapidly, with the endometrial surface being covered by epithelium growing out from the glands. Mitoses were frequent, the stroma was deciduallike in character. There was some evidence of chronic infection present.

*Nine-day post-partum specimen:* The surface now was covered completely by new epithelium from the glands which still showed excessive mitotic activity. The stroma was well maintained and was predecidual in type. The large clear nuclei of both the gland and stromal cells seemed to be characteristic. In the normal post-partum case, covering of the endometrial surface was not complete until twelve to thirteen days post partum.

*Ten-day post-partum specimen:* Here again was bridging epithelium, with the surface completely covered. The stroma was still predecidual in type, with a rare mitotic figure seen in the predecidual cells.

*Eleven-day post-partum specimen:* The surface was covered by adult epithelium. The stroma cells still were predecidual in type, more mitoses were seen, although they seemed to be losing some cytoplasm.

*Twelve-day post-partum specimen:* The glandular epithelium still showed evidence of mitotic activity, and occasional mitotic figures were seen in the surface epithelium of the endometrium. The stromal cells were predecidual, but were reverting now to a more basal type, with smaller, darker nuclei, and with less cytoplasm.

No more estrogen was given to one patient, who was followed nine days after withdrawal of hormone, and checked again fifteen days after withdrawal of hormone, or twenty-one and twenty-seven days post partum, respectively.

*Twenty-one-day post-partum specimen:* Mitotic figures still were present in the glands but were less numerous. The glands were non-

specific in type, with no secretory activity. Both the stroma and glands resembled those of the basal endometrium.

*Twenty-seven-day post-partum specimen:* Rare mitoses in glands, with simple glands and nonspecific stroma. The picture was one of early proliferative endometrium.

Certain estrogen effects are evident from these slides. First and most notable effect is that the covering of the denuded endometrial cavity is accomplished by the ninth day under estrogen effect, whereas normally this is accomplished by the twelfth to thirteenth day. This might be anticipated because of the greatly increased mitotic activity

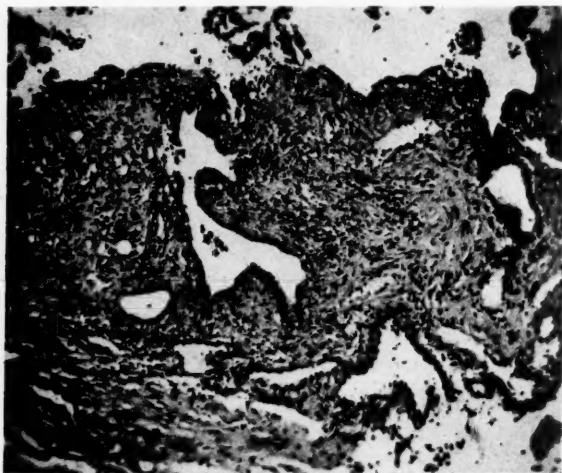


Fig. 1.—Normal nine-day post-partum endometrium. Epithelium is growing out from the gland stubs and has nearly completed the gap between glands. Stroma is non-specific basal in type. Glands are simple with cuboidal epithelium. Myometrium is well involuted.



Fig. 2.—Nine-day post-partum endometrium under female sex hormone influence. Epithelium has bridged the gap between the gland stubs. A mitotic figure is present in the surface epithelium. The stroma is predecidual in type. In other sections, gland epithelium has many mitotic figures with large nuclei, abundant cytoplasm. Myometrium as above.



throughout the entire endometrium, the glandular epithelium, the stromal cells, and even the surface epithelium as it grows outward. Mitotic figures are apparent in both the estrogen-treated group and in the normal post-partum group at four or five days in the glands, which re-cover the denuded surface by outgrowth of their epithelium.

Next of note is the fact that the stroma fails to return promptly to the nonspecific basal type seen in the normal post-partum group. The stroma is maintained as viable decidua or predecidua, in which under continued estrogen stimulation evidence of mitotic activity is seen. Ordinarily the post-partum decidua is sloughed as a superficial layer, with the deeper layer of spongy and basal decidua returning to the intermediate type of cell containing a small nucleus and relatively



Fig. 3.—Eleven-day post-partum endometrium under male sex hormone therapy. There is no evidence of epithelial activity, with bare myometrium in most areas. Glands are of simple cuboidal type with no mitotic activity. Myometrium involuting normally.

little cytoplasm. Such change did not take place here, but the decidua was maintained and even encouraged in proliferation by the estrogens. Promptly after estrogen withdrawal, the decidua regressed to its usual state, this being accomplished within eight days following estrogen withdrawal.

No change in myometrial regression was seen under estrogen effect. This was confirmed clinically as well by careful examination of uterine size at twelve days post partum. Involution grossly failed to differ from the normal.

Last of note is the absence of any evidence of infection or hemorrhage in this group of patients.

*Male Sex Hormone Influence, Endometrial Biopsies.*—These patients had been given orally 10 mg. daily of methyl testosterone, and each day represents an individual case.

*Three-day post-partum specimen:* There was little slough present, only a thin decidual layer, and burned-out glands were present. Recent thrombi were present in the vessels.



*Four-day post-partum specimen:* As above, only additionally, it was noted that the glandular epithelium had begun to change. There was slight swelling of the cytoplasm, the nuclei were pyknotic, and the cells themselves were somewhat irregular.

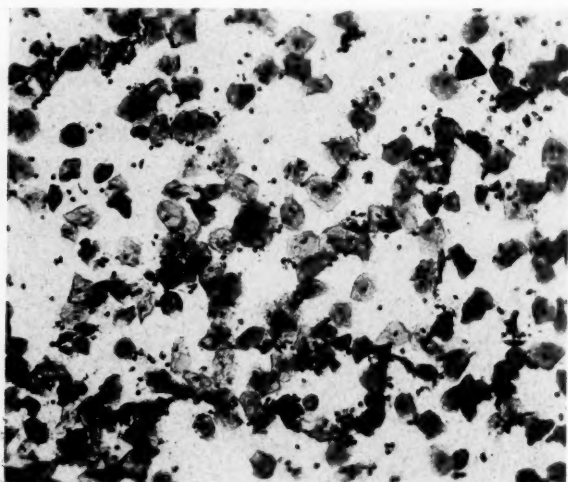


Fig. 4.—Normal ten-day post-partum vaginal smear. Abundant adult epithelial cells with small central nuclei, well-marked cytoplasmic margins, with only rare deep forms and but little debris.

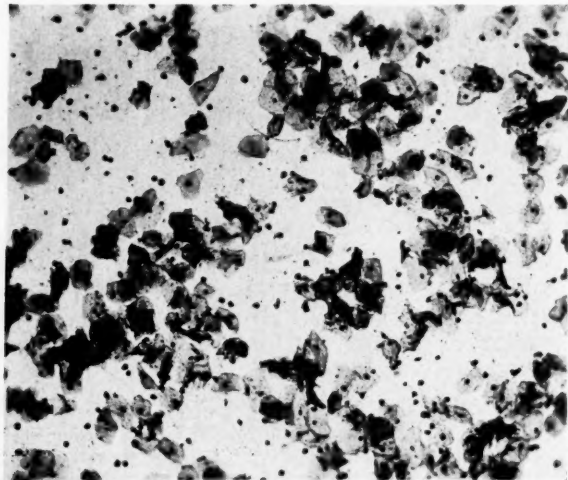


Fig. 5.—Ten-day post-partum vaginal smear under female sex hormone influence. Almost impossible to detect any difference between this smear and Fig. 4. Adult, well-delineated epithelial cells, little debris, with virtually no deep forms.

*Five-day post-partum specimen:* There were very little viable decidua left covering the myometrium, and there were a few glands left, with no mitoses present, and with the change noted above still present.

*Six-day post-partum specimen:* The glandular epithelium was cuboidal, much attenuated, with a rare mitotic figure present. The

stroma was nonspecific in type, extremely thin, and no decidua were recognizable except through the slough.

*Seven-day post-partum specimen:* The glandular epithelium was cuboidal, with nuclei which seemed large, clear, with swollen cytoplasm. The stroma was regressing and indifferent in type.

*Eight-day post-partum specimen:* There seemed to be no effort to cover the denuded myometrium. Only a scanty, resting stroma covered the myometrium. Infrequent glands were seen with pale, swollen nuclei; only a rare mitosis was present. A patch of involuting decidua still was present in this patient.

*Nine-day post-partum specimen:* Some effort to recover the surface was seen here, with simple epithelium growing out to cover partially the surface. Slough was present, with old hemorrhage. Both glandular epithelium and stroma were of simple resting type.

*Ten-day post-partum specimen:* There was virtually nothing covering the myometrium, yet there was no evidence of hemorrhage or infection.

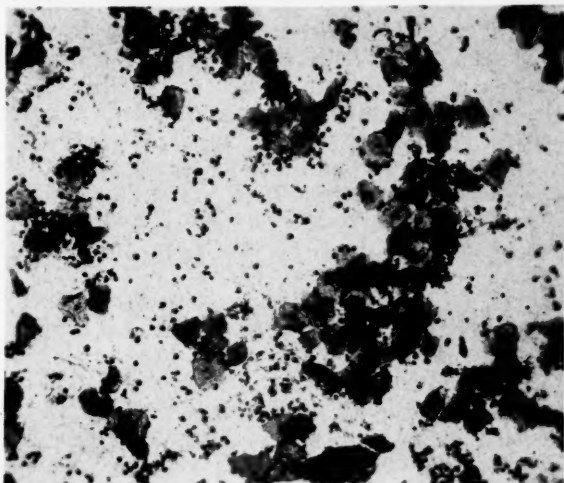


Fig. 6.—Ten-day post-partum vaginal smear under male sex hormone influence. Less florid smear, with many adult forms, but as well many less mature forms with larger nuclei, less cytoplasm. Some "boat-shaped" or navicular forms. Much more debris than in previous smears. This smear is suggestive of the partial castrate smear.

*Eleven-day post-partum specimen:* Only a few burned-out glands were present, usually as small nests of epithelium down in the myometrium, with rare mitoses. Stroma was nonspecific, greatly thinned out or absent in patches. There was no mitotic activity in the stroma, and no evidence of recovering of the surface to which were adherent fibrin, leucocytes, and slough.

*Twelve-day post-partum specimen:* No more effort was seen in covering the denuded surface. The gland stubs stop short at the myometrial surface, which in some areas was covered with but a few layers of basal-type stroma.

One patient was followed six, fourteen, and twenty-one days following withdrawal of the male sex hormone, or on the eighteenth, twenty-sixth, and thirty-third post-partum days.

*Eighteen-day post-partum specimen:* Glands were simple and pseudo-stratified in type, with few mitoses. The epithelium was undergrowing the slough which still covered the surface. Rare mitoses were seen in the stroma which now resembled basal stroma. Hemosiderin was seen in macrophages in the stroma. (This patient used three or four pads daily for the first three weeks post partum.)

*Twenty-six-day post-partum specimen:* The surface still was not epithelized, mitoses were present, as was hemosiderin in some macrophages.

*Thirty-three-day post-partum specimen:* The surface was covered by simple epithelium, the glands were proliferative in type with occasional mitoses present, and the stroma was nonspecific in character.

Certain androgen effects were evident from these slides. First and most significant effect was that of marked retardation of repair of the endometrial surface. This was not accomplished for the first twelve days post partum under hormone therapy, and it was not until the hormone had been withdrawn from for two to three weeks that epithelial resurfacing was completed. This was in contrast with the usual process completed by the twelfth to thirteenth post-partum day. Mitotic activity appeared on the usual fifth day, but was of little significance throughout the period of hormone influence.

No change in myometrial involution was detected microscopically, nor on clinical measurements of gross uterine size.

In only one case of the 12 was there increased lochia. Three or four pads daily were used for the first twenty-one days. This is probably of little significance. No clinical evidence or microscopic evidence of infection was present. Evidence of old hemorrhage was seen in 2 of the cases.

*Vaginal Smears, Normal and Hormone-Treated.*—Numerous reports from various investigators have described changes in the vaginal epithelium which accompany cyclical endocrine phenomena. Smears of the vaginal epithelium were prepared in all three series of cases, the normal post-partum group, the estrogen- and the androgen-treated groups.

Smears prepared from the normal post-partum group were largely those of "full estrogen effect" with adult epithelial cells, rare deep cells or leucocytes. Daily variations in the essential pattern were minimal although on the sixth post-partum day there is a sudden definite increase in the number of deep cells, either of the navicular type or the small round cell type. This is noted from the sixth to the tenth day, following which the smear reverts to the normal full estrogen effect type, with adult cells of large distinct cytoplasmic margins and small centrally placed nuclei. From the picture presented in both the endometrium and in the vaginal smear, it would seem that regeneration of the endometrium is under estrogen control. Mitotic figures appear in the gland epithelium about the fifth day which may mark a sudden resurgence of circulating estrogen from ovarian activity. At about this same time, however, the vaginal smear shows a slight increase in number of less mature surface epithelial forms. This has disappeared by the tenth day, but it is at variance with the endometrial pattern of increased mitotic activity present in the glands. However, it may be that the vaginal mucosa is a less sensitive instrument recording hormone variations, and that the relatively complete estrogen effect seen during the first four post-partum days is a carry-over from the higher

estrogen levels of pregnancy. As these influences are withdrawn, some five days later a florid desquamation takes place with the appearance of a slightly increased number of deeper cell forms. Following this, the less sensitive vaginal epithelium slowly returns to full estrogen effect from ovarian sources although this may not be complete until ten days post partum. Whatever the interpretation, nevertheless, it may be said that the vaginal epithelium normally presents the picture of a mature, resisting epithelial surface.

Under the influence of 10 mg. of diethylstilbestrol daily, orally, for the first twelve days, the vaginal epithelium consistently shows full estrogen effect, without the tendency noted above for a slight drop in adult forms. It is extremely difficult to tell the difference between the normal post-partum smears and the smears from the estrogen-treated group unless there possibly is a little less debris, a few less deep forms and leucocytes. This is noted consistently from the immediate post-partum smear onward. No therapeutic conclusions can be drawn.

Under the influence of 10 mg. of methyl testosterone daily, orally, for the first twelve days post partum, the vaginal epithelium resembles that of the normal post partum until the fifth or sixth day when there is a definite increase in the number of less mature forms and deep cells, and more leucocytes. This coincides with the appearance normally of these forms, and lends support to the impression that the vaginal epithelium is a less sensitive end organ for hormones than the endometrial tissues. The full estrogen effect of pregnancy is pictured by the vaginal epithelium for five or six days after it is withdrawn. Male sex hormone in the magnitude used in this study does not change this process, but as the deep forms appear normally, male sex hormone exaggerates the continuance and quantity of the less mature forms. This change is not seen in the patients under estrogen treatment. As the male sex hormone is continued, the smear comes to look more and more like that of testosterone effect or of partial castration. It never fully approaches the smear of a complete castrate or postmenopausal patient.

Within a week after male sex hormone is withdrawn, the vaginal smear is again that of full estrogen effect and continues so thereafter. No change from the normal is seen in estrogen-treated cases followed for some weeks. Practically, there is no apparent therapeutic significance in these findings, for repair of episiotomy incisions or vaginal lacerations proceeds at the average rate. Photomicrographs have been prepared demonstrating the appearance of the vaginal smear at ten days post partum in the normal and in the hormone-treated series.

#### DISCUSSION

If one breaks down into sequence the physiologic changes by which the post-partum endometrium is returned to the nonpregnant endometrium, three phases are noted: involution, repair, and regeneration. Normally, involution is completed within the first four or five days, repair occupies the next six or seven days with appearance here of mitotic activity, and regeneration proceeds from thence onward.<sup>6</sup> If the patient is lactating, the endometrium remains in the completely regenerated, resting phase until ovulation ensues either while the patient is still lactating, or after this function has concluded. If the

patient is not lactating, ovulation occurs on the average at six weeks, with menstruation some fourteen days later.

The efficiency with which this natural process is consummated is common knowledge. Only the rare case requires medical aid. However, under estrogen treatment the process of involution seems retarded, for the glands are maintained at a high level and under forced draft re-epithelize the mucosal surface by the eighth or the ninth day; some 25 per cent quicker than is normal. Mitotic activity is greatly increased in the glandular epithelium. The stroma is not allowed to involute, but is maintained as decidua or as predecidua, with actual proliferation induced in these cells as evidenced by mitotic activity. The swollen cytoplasm, large clear nuclei, and mitotic figures present in both these elements are unmistakable. It may be suggested that the basal zone of endometrium is the last to change into decidua and is the quickest zone to regress after pregnancy is terminated. Under estrogen stimulation, this zone may not be allowed to regress, but proliferation is forced while it is still in its predecidual or decidual phase. Many variations are noted under estrogen treatment, from the bare nuclei of undifferentiated stroma to predecidua or decidua. Each patient is to be allowed her individual variations, but the general trend is unmistakable.

After estrogen is withdrawn, glandular and surface epithelial activity shades off as it normally does. However, a full week is necessary before the stroma regresses from its decidual form into the basal type. The more rapid covering of the denuded endometrium clinically may have lowered the incidence of post-partum morbidity.<sup>2</sup> Whether the stimulus given by estrogens to epithelial activity is dangerous is a difficult question, had the patient retained trophoblastic tissues, or had abnormal trophoblastic tissue been present and viable.

Under androgen therapy, the process of decidual involution is unchanged, but repair is brought almost to a standstill. Effort to resurface the denuded myometrium is alarmingly slight, and but little is made until the androgen is withdrawn. Three weeks after withdrawal, the surface is epithelized, but during this period resistance of the endometrium to infection may be lessened and the possibility of bleeding may be greater.

Under neither agent, however, was myometrial regression affected, either on the basis of clinical or microscopic evidence.

#### SUMMARY AND CONCLUSIONS

1. Three different groups consisting of 12 patients each were studied by endometrial biopsy and vaginal smear during the puerperium. One group was normal post-partum patients and each supplied a single day's picture. A second group of normal post-partum patients was given 10 mg. of diethylstilbestrol orally for the first twelve post-partum days, each patient giving only one endometrial biopsy and one vaginal



smear. A third group of normal post-partum patients were given 10 mg. of methyl testosterone orally for the first twelve post-partum days, each patient giving only one endometrial biopsy and one vaginal smear.

2. These hormone-treated patients demonstrated definite variations from the normal processes of involution, repair, and regeneration.

3. Involution was delayed by female sex hormone, but not by male sex hormone.

4. Repair was hastened by female sex hormone, but markedly retarded by male sex hormone.

5. Regeneration was hastened for covering of the surface epithelium by female sex hormone, but stromal regeneration was delayed. Regeneration was delayed by male sex hormone.

6. The effects of female sex hormone were lost within one week after withdrawal, and the effects of male sex hormone were lost within three weeks after withdrawal of the hormone.

7. Certain theoretical questions regarding the use of either agent in the puerperium are raised.

Acknowledgment is made to Dr. Arthur T. Hertig and to Dr. Frederick C. Irving, for critical review of this paper. The following are thanked for their experimental grants of the following: E. 391 (oral), diethylstilbestrol, Department of Medical Research, Winthrop Chemical Co. Oretone—M (oral), Methyl testosterone, Schering Corporation, Dr. Max Gilbert, Mr. R. W. St. Clair, the latter of whom supplied the excellent photomicrographs. Metandren (oral) methyl testosterone, Ciba Pharmaceutical Products, Mr. E. O. Paden.

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**Ishmael, William K.:** *Menopausal Arthralgia*, *J. Lab. & Clin. Med.* 27: 297, 1941.

The diagnosis of menopausal arthralgia can be made only if rheumatic symptoms dating back to the age of the menopause completely yield to appropriate treatment.

In the fairly large series reported by Ishmael, he applied as general supportive measures: diet, avoidance of trauma, avoidance of unfavorable climatic factors, leaving foci of infections intact, administering supplementary vitamins, correction of disturbances of metabolism, of gastrointestinal function, of emotion, posture, etc., and finally relief of pain. Added as specific measures are: estrogenic substances, autohemotherapy, and artificial fever. He also made use of physical therapy and orthopedic measures.

Analyzing his results he concludes that stilbestrol should preferably supplant the use of the estrogenic hormone.

HUGO EHRENFEST.

## CLINICAL EXPERIMENTS IN RELATION TO THE EXCRETION OF THE ESTROGENS\*

### II. FUNCTIONAL FLOWING. URINARY ESTROGENS BEFORE, DURING, AND AFTER PROGESTERONE, ESTRIOL, AND CYCLIC ADMINISTRATION OF PROGESTERONE AND ESTRADIOL BENZOATE

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#### INTRODUCTION

THE patient upon whom these studies were made began having functional flowing in 1930, three months after the onset of menstruation at the age of 15. Curettage had been performed twice before she came to the Free Hospital for Women in January, 1934. No organic disturbance except abnormal uterine bleeding and secondary anemia has been discoverable during the eight years that she has been cooperating with us in attempts to cure her disability by conservative measures. Seven times, through January, 1938, have specimens of endometrium showed marked hyperplasia.

She has taken large quantities of ferrous sulfate for anemia. Estrogens, chorionic gonadotropin, progesterone (in amounts which we now recognize as inadequate), wheat germ oil, anterior pituitary extract, and oral placental extract (Eley) have been tried and repeated with little or no discernible therapeutic effect on her bleeding, which has duplicated every pattern of functional flowing.

In July, 1934, curettage, resection of a 3 cm. thecal luteal cyst of the left ovary, appendectomy, and uterine suspension were performed. Nearly four months of amenorrhea ensued. Intrauterine application of well-screened radium, 300 mg. hours, given in April, 1935, for recurrent bleeding, was followed by amenorrhea of six months' duration, and then a recurrence of the disorder in the form of irregularly occurring, prolonged spells of staining without excessive loss of blood. The patient married in June, 1936.

Urinary estrogens were measured in January, 1938, before, during, and after the parenteral administration of fairly large doses of progesterone and estrone. This study has been reported.<sup>6†</sup> Thereafter came four months of amenorrhea and then intermittent staining interspersed with one- to ten-day spurts of flowing.

\*Presented in brief before the New York Obstetrical Society on January 13, 1942.

The Mrs. William Lowell Putnam Investigation of the Toxemias of Pregnancy, aided by grants from the Committee on Research in Problems of Sex of the National Research Council.

†All references will accompany the fourth paper of this series.

Although the basal metabolic rate was normal, thyroid extract, one-half a grain three times a day, was prescribed and taken faithfully from November, 1938, through September, 1941. From March through November, 1939, the patient had periods, at twenty-seven- to thirty-six-day intervals, varying from a day of staining to six days of profuse flow. After two months of amenorrhea and a month of staining, came a profuse flow and then three episodes of staining at thirty-three- to thirty-five-day intervals. Increasingly profuse flow starting in August, 1940, brought the patient to the hospital late in November, 1940, at the age of 25, when the studies and therapies herein reported were begun. At that time her hemoglobin was 42 per cent by the Sahli method.

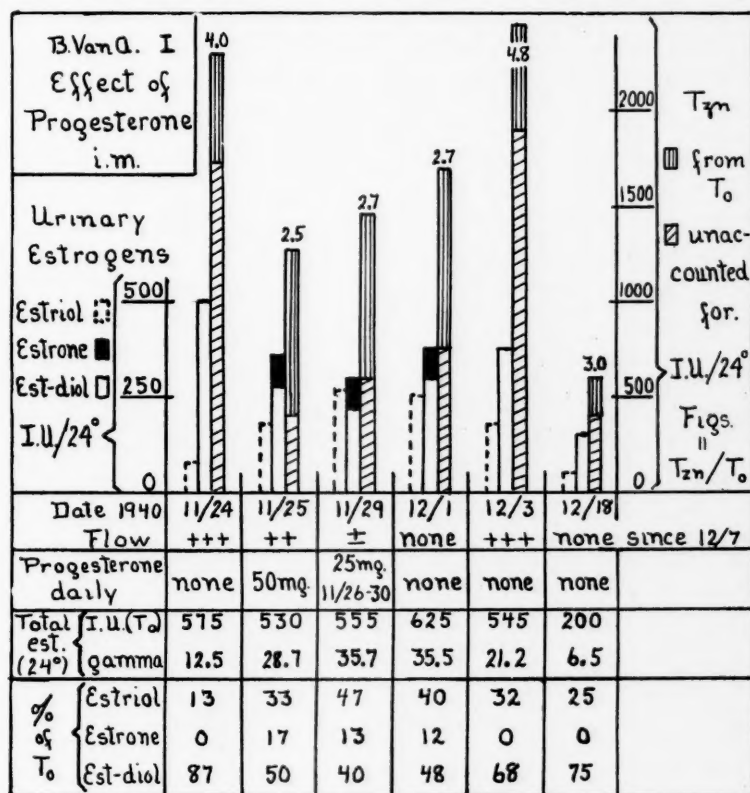


Chart 1.

## THERAPY WITH PROGESTERONE ALONE (CHART 1)

For the methods of urinalysis employed and for explanation of the charts, the reader is referred to the first paper of this series. "Unaccounted for"  $T_{zn}$ , that is, the estrogenic activity of urine after zinc-hydrochloric acid hydrolysis which cannot be accounted to the estrogens already present, as well as  $T_{zn}$  to  $T_0$  ratios appear to provide considerable information concerning estrogen destruction. Total urinary estrogens are expressed both in activity units (I.U.) and by weight (micrograms), the latter being calculated on the basis of standardization

assays of crystalline estradiol, estrone, and estriol. Twenty-four- to forty-eight-hour specimens were extracted, but all results are expressed in terms of twenty-four-hour excretion for the sake of comparison.

Bleeding necessitated the use of a retention catheter for collecting urine. Absence of estrone, a high percentage of activity in the estradiol fraction, and a marked increase in the estrogenic potency after zinc-hydrochloric acid hydrolysis featured the control specimen. This is the typical partition of urinary estrogens at the time of menstruation, both normal and abnormal. To us these findings reflect more rapid degradation of estrogens and restricted estradiol to estrone to estriol conversion, these processes in turn reflecting reduced or absent steroids of the progesterone type.

Specific treatment with really adequate amounts of progesterone\* retarded and finally stopped the flow. No change in the total estrogenic potency acquired by simple hydrochloric acid hydrolysis of the urine resulted but in terms of weight two to three times as much estrogenic substance was excreted, the reason being that progesterone caused conversion of the more active estradiol to less active estrone and estriol and retarded degradation, as further indicated by the reduction of the "unaccounted for" potency after zinc-hydrochloric acid hydrolysis. Since estrone is the most labile of the known estrogens, its appearance was still further evidence that progesterone had depressed the degradation mechanism. These results confirm previously reported findings on this same patient<sup>6</sup> by providing direct evidence for the role played by progesterone in decreasing the rate of estrogen degradation and facilitating estradiol to estrone to estriol conversion.

Sixty hours after the last injection a profuse progesterone-withdrawal period began, on the second day of which the amounts and partition of the urinary estrogens were essentially similar to those before treatment. Fifteen days later, eleven days after the end of the period, the only significant change in the urine was the reduced values indicating reduced ovarian activity.

#### A TRIAL OF ESTRIOL ORALLY (CHART 2)

Our object in this study was to put the ovaries at rest temporarily in the hope that a return to normal function would ensue. Estriol† was chosen because we desired to learn more about its fate after ingestion. It was taken in alcoholic solution from Dec. 20, 1940, through March 14, 1941, the daily dose being increased from 0.5 to 1.0 mg. on January 20 and to 2.0 mg. on March 4.

Good absorption and, compared with estrone and estradiol, considerably less destruction are indicated by the urinary recovery of 24 to 37 per cent. Similar recoveries of orally administered estriol have been obtained in three other patients. Such relatively high recovery is in keeping with its known greater stability. Furthermore, the  $T_{zn}$  to  $T_o$  ratios during treatment are the lowest we have ever found in this patient and signify to us that the degradation process was being retarded, not only because of the stability of estriol but also possibly because of the

\*Proluton, a product of the Schering Corporation.

†Theolol, a product of Parke, Davis & Company, through the courtesy of Dr. E. A. Sharp.

greater quantity of steroid present. In view of this evidence for decreased destruction, the failure to find any estrone in these specimens shows that estradiol to estrone conversion was being prevented. Though contrary to our thesis concerning the favorable effect of decreased destruction upon conversion, prevention of conversion in this instance would be expected according to the law of mass action since the concentration of the end product of the estradiol to estrone to estriol reaction was raised. Also, since there was a decrease in excreted estradiol during the first six weeks of the experiment and no later increase commensurate with the augmentation of estriol, it appears that neither estrone nor estradiol is formed from estriol, as was shown in earlier work on rabbits.<sup>12, 13</sup>

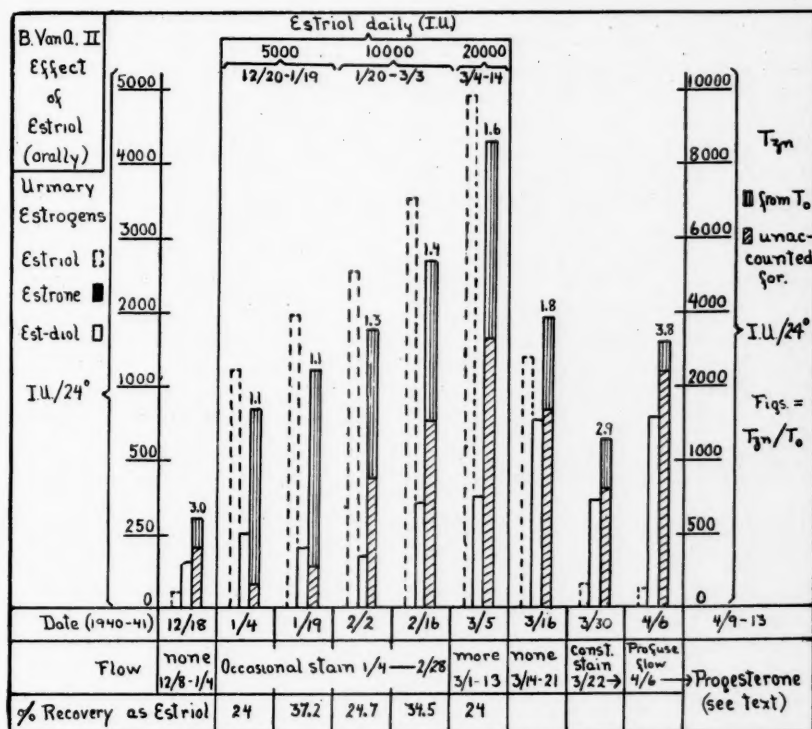


Chart 2.

A constant increment, after the first month of estriol medication, may be noted both in the  $T_{zn}$  to  $T_0$  ratio and in the amount of "unaccounted for" activity after zinc-hydrochloric acid hydrolysis. Two interpretations of this observation are possible. The fact that this increment was associated with an increased excretion of estradiol (presumably the primary ovarian hormone) suggests that, despite the larger dosages of estriol, greater ovarian secretion was taking place at this time. On this basis the higher  $T_{zn}$  to  $T_0$  ratios and greater amounts of "unaccounted for"  $T_{zn}$  activity may have come from estradiol breakdown products. On the other hand, although cessation of estriol administration was followed by a considerable augmentation of estradiol excre-



tion, indicating increased ovarian activity, and a continued rise in  $T_{zn}$  to  $T_o$  ratios, evidence for more estrogen breakdown, there was a drop in the amount of "unaccounted for"  $T_{zn}$  potency. This suggests that during estriol medication at least part of the "unaccounted for" value came from reactivation of estrogenically inactive estriol metabolites. One might interpret the steady increment in  $T_{zn}$  activity during the latter part of the period of medication, therefore, as indicating that continued and increasing dosage of estriol, although not affecting the recovery of estriol as such, resulted in less complete degradation so that a larger percentage of inactive estriol metabolites could be reactivated.

Although the evidence after cessation of estriol ingestion points to more ovarian activity and therefore to a certain amount of ovarian inhibition during therapy, the presence of urinary estradiol during the medication period in amounts above the control and the patient's continued functional flowing show that the object of the experiment, complete ovarian inhibition, was never accomplished.

We have since discovered that the daily ingestion of 2.5 mg. of estriol failed to affect the cycles of a sterile patient and that 1 to 5 mg. daily for three and one-half months failed to affect the cycles or pain of another patient with essential dysmenorrhea. When this last patient, however, took 15 mg. of estriol daily starting on the fourteenth day of the cycle, menstruation was forestalled until the fortieth day, two days after the last dose.\* Biddulph and his associates,<sup>14</sup> working with parabiotic rats, have shown that sixty times as much estriol is required to suppress the castrate pituitary as estradiol. We wonder whether the comparative ineffectiveness of estriol in influencing pituitary-ovarian activity may not be related to the greater resistance of this estrogen to degradation in the body. We have stated our reasons<sup>8</sup> for believing that the pituitary-ovarian effects of estrogen may be accountable to degradation metabolites rather than to estrogens themselves.

Because the patient's excessive bleeding which started on April 6 showed no sign of letting up, progesterone, 25 mg., was given daily from April 9 through April 13, inclusive. Flowing decreased but did not completely stop during injections. Profuse flow started again two days after the last injection and ceased entirely five days later.

CYCLIC ADMINISTRATION OF PROGESTERONE AND ESTRADIOL BENZOATE  
(CHARTS 3 AND 4)

Although withdrawal bleeding may be produced in both monkeys and women with estrogens alone, it is becoming increasingly apparent that progesterone is a very much more effective agent than the estrogens in the control of endometrial flow.<sup>15-17</sup> In our own experience and that of others, it has been noted that, whereas estrogen withdrawal may result in anything from no flow at all to prolonged and uncontrolled bleeding, progesterone and estrogen withdrawal is almost invariably followed by an amount and type of flow which parallel the normal catamenia. Since animal investigation and our own studies on women<sup>6-10</sup> have shown that

\*This period was more profuse and much less painful than usual. It would appear that the luteal phase of the cycle was prolonged by this large daily dose of estriol. The consequent symptomatic relief is in keeping with the hormonal findings on this patient which are reported in the third paper of this series.

estrogen is necessary for the optimum effect of progesterone, the administration of estrogen together with progesterone in cases of progestin deficiency is rational, and has indeed been found<sup>10, 16, 17</sup> to augment the effectiveness of progesterone therapy. Because of the above considerations and because of the known retroactive effect of ovarian secretions upon the pituitary, it was decided to produce cyclic estrogen and progestin-withdrawal bleeding in this individual, in the hope not only of controlling her abnormal flow but of establishing a normal cyclic pituitary-ovarian relationship which would continue after cessation of the artificially-produced condition. This form of therapy in functional

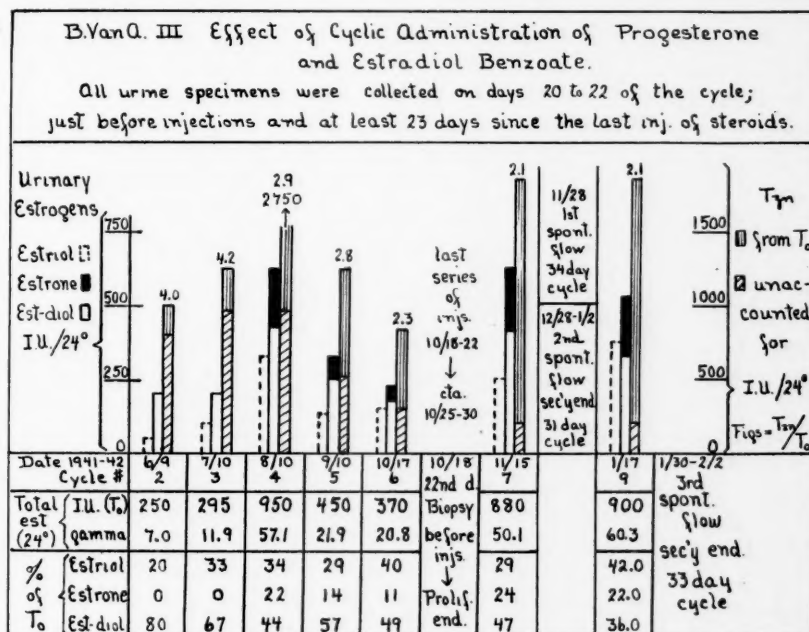


Chart 3.

flowing has already been reported upon favorably by Hamblen.<sup>17</sup> We were particularly interested in determining whether or not any resultant spontaneous ovarian control would be reflected in a more normal metabolism of the ovarian steroids as gauged by the urinary metabolites.

On May 5, twenty days from the start of the April progesterone-withdrawal period, 10 mg. of progesterone and 1.25 mg. of estradiol benzoate\* were given intramuscularly, this dosage being repeated for five consecutive days. On May 19, ten days after the last injection, a normal five-day period began. It was decided, because of the prolonged interval between injections and the start of flow, that less estrogen should be administered. Beginning on June 10, therefore, twenty-two days from the start of the previous flow, five daily doses of 10 mg. of progesterone and 0.33 mg. of estradiol benzoate were injected. Withdrawal flow

\*Proluton and Progynon-B, supplied by the Schering Corporation.

started on June 20, six days after the last injection. This procedure was repeated exactly in July and August, each series of injections being started on the twenty-second day from the start of the last period and resulting in normal flow six days after the last injection. In September the same timing of injections was adhered to, but twice as much estradiol benzoate was given. This was followed by a twelve-day interval between the last injection and the start of flow, making a thirty-eight-day interval between catamenia rather than the thirty-one-day intervals

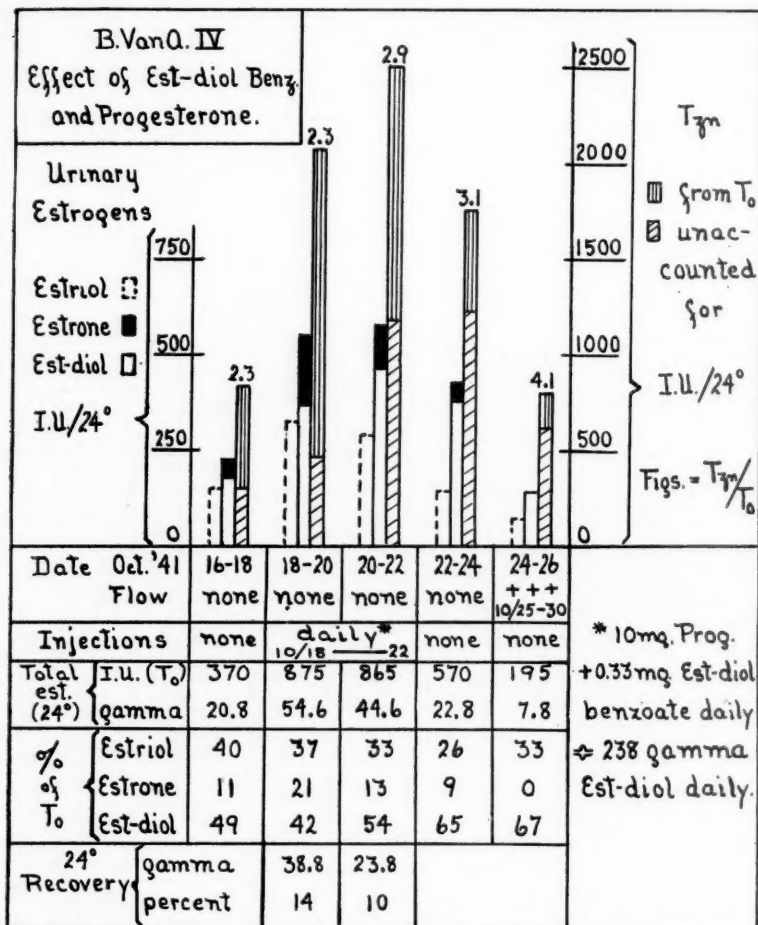


Chart 4.

which had resulted from the three previous cycles of therapy. It seems apparent that estrogen overdosage prolonged the interval between injections and withdrawal bleeding. The seventh and last series of injections, 10 mg. of progesterone and 0.33 mg. of estradiol benzoate daily for five days, was started on Oct. 18, 1941, the twenty-second day since the start of the September period. A five-day period began on October 25, three days after the last injection, making a twenty-eight-day interval between catamenia.

An endometrial biopsy on October 18, before this last series of injections and on the twenty-second day of the cycle, showed normal proliferation with no evidence of secretory change. Therapy was discontinued. On November 28, the thirty-fourth day since the last catamenia, the patient spontaneously bled for one day only. Thirty-one days later a spontaneous normal five-day period occurred, a biopsy taken at the start of flow revealing secretory endometrium with predecidual change. On Jan. 11, 1942, the fourteenth day of the cycle, a slight stain was noted. On January 30, the thirty-third day since the December period, a normal five-day catamenia occurred. A biopsy at the start of flow again revealed secretory glands and predecidual changes. The patient is still (seven months since the last series of estrogen and progestin injections) having normal catamenia at thirty to thirty-three-day intervals with no intermenstrual bleeding.

Beginning in June, 1941, after two artificially-produced withdrawal catamenia, forty-eight-hour specimens of urine were studied, covering the twentieth to twenty-second day of each cycle (Chart 3). These specimens were all collected before any hormones were given and at least twenty-three days from the last series of injections. The findings, therefore, must reflect spontaneous ovarian activity.

In the June and July specimens the absence of any demonstrable estrone, the high percentage of activity in the estradiol fractions, the high  $T_{2n}$  to  $T_o$  ratios, and the large amounts of "unaccounted for"  $T_{2n}$  activity all reflect the rapid degradation and failure in conversion of secreted estrogens indicative of progestin deficiency. Including four specimens of the 1938 study,<sup>6</sup> these make a total of eleven urinalyses on this patient, when no hormones were being administered, in which the same partition of estrogen metabolites has pertained, seven having been collected during flow and four when the patient was not bleeding. This consistency makes the change in urinary findings in August and the following months of unquestionable significance.

Beginning in August, after the fourth artificially-produced menstruation, goodly amounts of estrone became demonstrable in the urine, the percentage of activity in the estradiol fractions decreased, the  $T_{2n}$  to  $T_o$  ratios became lower, and there was a progressive decrease, with each cycle, in the amount of "unaccounted for"  $T_{2n}$  activity. Although a biopsy on the twenty-second day of the October cycle showed only proliferative endometrium and although the first spontaneous period (in November) was extremely scant, we feel justified in assuming, on the basis of the urinary findings, that spontaneous cyclic ovarian secretion of progestin was occurring from August on, even though ovulation may not have occurred. Hisaw<sup>15</sup> has recently stated our own conviction that absence of ovulation or of an endometrium which may be considered histologically as secretory does not necessarily mean complete absence of luteal function. In fact, the preovulatory partition of estrogen metabolites in the normal cycle<sup>6, 11</sup>, and the third paper of this series suggests that some luteal secretion may precede rupture of the ovarian follicle.

No urine was collected in December preceding the second spontaneous flow which we know, from the biopsy, was postovulatory. A forty-eight-hour specimen in January on the twentieth to twenty-second day of the cycle, five days after "ovulation" staining and twelve days before another spontaneous\* catamenia from a secretory endometrium, showed amounts and partition of estrogen metabolites which point to the most



complete conversion and the least destruction of secreted estrogen that we have ever found in this individual. Even when 50 mg. of progesterone were given (see November 26, 1941, Chart 1), there was a higher percentage of activity in the estradiol fraction and less in the estrone, and the recovery of "unaccounted for" activity after zinc-hydrochloric acid hydrolysis was greater. One might surmise that during the luteal phase of an ovulatory cycle this patient's ovaries secrete more than 50 mg. of progesterone in twenty-four hours.

In Chart 4 are presented the results of urinalyses during the last estrogen and progesterone treatment. All urine passed from forty-eight hours before the first injection through the ninety-sixth hour after the last injection was saved in forty-eight-hour batches. Menstruation started eighty hours after the last injection.

The recovery of the injected estradiol is approximated by using the control specimen as the base line and assuming that the benzoate ester was broken down in the body into a corresponding weight of  $\alpha$  estradiol. The figures indicate that  $\alpha$  estradiol, even in the presence of fairly large amounts of progesterone, is more rapidly destroyed than is estriol (see Chart 2). Its recovery, however, is four to five times as great as that of estrone alone administered to a menopausal patient (see first paper of this series, p. 455, September issue of JOURNAL) and about twice as great as that of estrone when given with progesterone to this same individual in January, 1938.<sup>6</sup> These comparative recoveries are in keeping with the known comparative stabilities of these estrogens and with the protective action of progesterone against their destruction.

Some estrogen conversion prior to the last injections is indicated by the partition of the urinary estrogen metabolites. This partition is similar to that found during the follicular phase of a normal cycle (see Chart 1 of the third paper of this series), whereas the specimen was collected on the twentieth to twenty-second day. A biopsy at the end of this collection period and before the first injection revealed a proliferative endometrium. The urinary findings during and after injections in this experiment approach those of the luteal and premenstrual phase of the normal cycle<sup>6</sup> and Chart 1 of the third paper of this series and provide good evidence that an hormonal and endometrial situation similar to the normal was being artificially produced. The changes observed after injections were stopped are illustrative of the effect of estrogen and progesterone withdrawal upon estrogen metabolism. The increased rate of estrogen degradation just before and at the start of flow is the same as that observed at the onset of normal postovulatory menstruation,<sup>6</sup> and Chart 1 of the third paper of this series.

Thus, according to the data, we were reproducing at regular intervals in this patient a normal situation which would not otherwise have pertained. We are inclined to the opinion that the *rapid* shift in estrogen metabolism which has been found consistently in our studies to follow estrogen and progestin withdrawal is concerned not only with the onset of flow but with the pituitary stimulation necessary for starting the ovary on a new cycle. By artificially supplying this stimulation seven consecutive times at intervals which approximated those of the normal cycle, we believe that the pituitary-ovarian discord from which this patient had been suffering since puberty twelve years ago was finally



interrupted. That the clinical success of this experiment was post hoc is indicated by the complete clinical history of the case as well as the urinary findings.

#### SUMMARY AND CONCLUSIONS

A patient whose menstrual history since puberty has duplicated every pattern of functional flowing has been studied and treated for eight years. The results herein reported cover the past sixteen months, during which large amounts of progesterone have twice been given to control profuse flow, estriol has been ingested over a three-month period in the hope of inhibiting ovarian activity, and seven series of progesterone and estradiol benzoate injections have been given cyclically, these finally accomplishing the desired objective, namely, the establishment of spontaneous and regular ovulatory cycles.

Urinalyses for estrogen metabolites throughout this investigation have confirmed previously reported conclusions concerning estrogen and progestin metabolism in women and have led to the following general conclusions: (1) Functional flowing is associated with a progestin deficient metabolism of estrogen and results from fluctuations in ovarian secretion in the absence of adequate luteal control; (2) progesterone, in large amounts, constitutes a specific therapeutic agent for the production of a more normal estrogen metabolism and the control of functional bleeding; (3) estriol, although well absorbed from the intestinal tract and less rapidly destroyed than estradiol or estrone, is comparatively ineffective, possibly because of its relative stability, in influencing pituitary-ovarian activity; (4) estrogen and progesterone withdrawal results not only in normal endometrial bleeding but in a sudden increase in the rate of estrogen destruction which may provide a necessary stimulus for the normal growth and maturation of ovarian follicles; (5) if this stimulus is artificially supplied at monthly intervals, a normal pituitary-ovarian cycle may be established which will continue after cessation of cyclic therapy.

*(The third and fourth sections of this presentation will follow in an early issue.)*

## GLOMERULAR FILTRATION AND RENAL BLOOD FLOW IN THE HYPERTENSIVE WOMAN AND IN POSTTOXEMIC HYPERTENSION

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IT HAS been repeatedly shown that hypertensive disease is characteristically accompanied by a reduction of renal blood flow<sup>1-3</sup> and a relative increase in glomerular filtration.<sup>3, 4</sup>

Chesley<sup>5</sup> has studied a number of women with hypertension following toxemias of pregnancy and has determined the renal blood flow by the diodrast clearance and the glomerular filtration by the urea clearance. A comparison of the values obtained for the posttoxemic hypertensive patient with those for hypertensive women who had never had toxemic pregnancies showed a moderate reduction in filtration in the former. These findings led him to believe that hypertension in the posttoxemic woman differed in etiology from that in the male or nonparous female with essential hypertension.

In Chesley's series the renal blood flow was determined by the diodrast clearance and the glomerular filtration by:  $\text{Urea clearance} / 0.60 = \text{Glomerular filtration}$ . This relationship is shown to be true in the average normal kidney in both dog and man<sup>6, 7</sup> but in the presence of renal damage the ratio of urea clearance to inulin clearance varied from 0.33 to 0.88.<sup>8, 9</sup> Chassis and Smith<sup>7</sup> sum up the use of the urea clearance in renal disease by stating that "as kidney damage decreases the ability of the kidney to resorb water, the urea clearance approaches the inulin clearance." If the hypertensive kidney is not normal, it would seem reasonable to suppose that the use of the urea clearance for the determination of glomerular filtration might lead to considerable error.

The high incidence of residual hypertension in patients having had toxemic pregnancies and the inability to demonstrate an increased incidence of hypertension in parous women when compared to nonparous women in any age group,<sup>10</sup> make it seem likely that the diseases in the male, female, and posttoxemic hypertensive are related. It has been demonstrated that renal blood flow is reduced post partum in the toxemias of pregnancy, while the glomerular filtration rises,<sup>11, 12</sup> thereby giving a picture similar to hypertensive disease. We<sup>13</sup> have been able to show normal filtration rates for posttoxemic patients with normal blood pressure readings.

## MATERIALS AND METHODS

Our series included 23 patients who were divided into two groups. The nonparous hypertensive group consisted of 10 patients who had blood pressure levels of 150-240/90-170, the average level being 185/110. The posttoxemic group consisted of 13 women who were known to have had pregnancies complicated by hypertension and albuminuria and whose records during these pregnancies are available since all had been delivered in the old or new lying-in Hospital of New York. The blood pressure readings varied from 130-230/90-130, averaging 157/100.

All patients were thoroughly studied clinically and examination of eye grounds, heart, and vascular status made. They varied in age from 23 to 61 years, and the toxemic patients had been pregnant from 1 to 39 years previously.

All clearances were run by two individuals and the method was standard. One thousand cubic centimeters of water were given by mouth the night preceding the test and 200 c.c. more were given at 5:00 A.M. and 6:00 A.M. At 6:00 A.M. the bladder was catheterized with a No. 14 soft rubber catheter and an intravenous drip started at 4 c.c. per minute, containing 15 c.c. of 10 per cent inulin and 10 c.c. of diodrast in 500 c.c. of 5 per cent glucose. A priming dose of 10 c.c. of 10 per cent inulin and 1 c.c. of diodrast was given at the beginning of the infusion. After twenty to thirty minutes the urinary bladder was emptied by washing two or three times with 20 to 30 c.c. of distilled water, and this was evacuated by inflating the bladder once with 50 to 100 c.c. of air. Clearance periods varied from ten to thirty minutes and an attempt was made to secure 80 to 120 c.c. of urine during each period. Three consecutive clearance periods were run on each patient. Blood values were determined in the midpoint of each the first and third clearance periods and the value of the second calculated by interpolation.

All determinations of blood levels were done on plasma except for blood urea which was made on whole blood. The inulin values on plasma and urine were done following incubation with 20 per cent yeast solution and precipitation with Somogyi's technique, by the method of Alving, Rubin, and Miller.<sup>14</sup> Diodrast was determined after precipitation of the plasma by 10 per cent trichloroacetic acid by the method of Alpert,<sup>15</sup> and this method was used on the urine in dilution of 1:250. Urea was determined on both the blood and the urine in 1:10 dilution by Van Slyke's manometric method<sup>16</sup> and uric acid in plasma and urine by the Folin technique.<sup>17</sup>

All clearances which failed to check within 10 per cent of the mean of the three clearances were discarded and all were recalculated on the basis of 1.73 square meters of surface area.

The filtration fraction was determined by  $\frac{\text{Inulin clearance}}{\text{Diodrast clearance}}$  and the renal blood flow by  $\frac{\text{Diodrast clearance}}{1 - \text{Hematoerit}}$ .

We have noted both in this series and in patients previously tested<sup>11, 13</sup> that on some occasions the urea clearance has shown higher values than the inulin clearance. This difference has generally been within the error of the method, which we feel is not less than 10 per cent on

any one clearance. We have not discarded these values in any instance in which they check within 10 per cent of the mean of the clearances run on that patient.

#### RESULTS

*Hypertension Occurring in Nonparous Patients.*—(Table I.) The inulin clearances in this group of patients averaged 82 c.c. per minute, with a range of 54 to 150 c.c. per minute. The diodrast clearances averaged 409 c.c. per minute and the renal blood flow was calculated at 675 c.c. per minute. The filtration fraction was 21.6 as determined by the inulin clearance but when calculated from the urea clearance/0.60, it was found to be 23.6. The average urea clearance was 58.0 c.c. per minute and the uric acid clearance averaged 23 c.c. per minute.

*Posttoxemic Hypertensive Women.*—(Table II.) The inulin clearance in this group was found to average 93 c.c. per minute. The diodrast clearances averaged 434 c.c. per minute and this gave a calculated renal blood flow of 720 c.c. per minute. The filtration fraction as determined from the inulin clearance was 21.7 but determined from the urea clearance/0.60, was found to be 29.0. The average urea clearance was 75 c.c. per minute, and the uric acid clearance averaged 30.7 c.c. per minute.

#### DISCUSSION

All of our "posttoxemic" women are classified by this broader term rather than into the subgroups of mild pre-eclampsia, severe pre-eclampsia, hypertensive disease, or renal disease, because we were unable to obtain previous renal function tests, eye ground examinations or satisfactory follow-up examinations of blood pressure and urine. We realize that each of these syndromes may in itself be an entirely separate clinical and pathologic entity.

The average age of the posttoxemic women is moderately lower than that of the nonparous group. The nonparous group, as is to be expected, seems to have more evidence of vascular and renal changes when one compares the blood pressure levels (185/110 in the nulliparous group as compared to 157/100 in the parous) and urea clearances in the two groups (58 c.c. per minute for the nulliparous and 75 c.c. per minute for the parous group). In spite of this apparent difference in vascular and renal status, there is no real difference in the glomerular filtration, renal blood flow, or filtration fraction.

Our glomerular filtration values as determined by inulin clearance are noticeably lower than those of normals (116 c.c. per minute) and also than those of Chesley<sup>5</sup> (106 c.c. per minute, urea/0.60) and Friedman<sup>3</sup> (104 c.c. per minute, clearances on 4 women). The diodrast and renal blood flow values (675 to 720 c.c. per minute renal flow) in general compare favorably with those of the above workers in both male and female hypertensives and seem to be merely proportional to the level of the blood pressure and to the length of time hypertensive and post partum. When the glomerular filtration is determined by urea clearance/0.60, we find that the parous women have a high filtration

TABLE I. CLINICAL DATA AND TABULATION OF CLEARANCE VALUES ON PATIENTS WITH HYPERTENSION.  
NONE OF THESE PATIENTS HAD BEEN GRAVID

PATIENT	AGE	PARITY	BLOOD PRES-SURE	AL-BUMIN	HEMA-TOCRIT	INULIN CLEARANCE C.C./MIN.	DIODRAST CLEARANCE C.C./MIN.	RENAL BLOOD FLOW C.C./MIN.	UREA CLEARANCE C.C./MIN.	URIC ACID CLEARANCE C.C./MIN.	FILTRATION FRACTION	UREA 0.60	UREA F.F.
1A	40	0-0-0	150/90	Neg.	40	110	670	1033	42.9	10.2	0.18	68.8	0.102
2A	43	0-0-0	160/100	Neg.	32	97	460	680	89.0	9.8	0.22	148.0	0.351
3A	44	0-0-0	240/170	+	40	54	150	250	23.7	15.9	0.25	48.7	0.336
4A	44	0-0-0	180/100	Neg.	41	80	556	942	61.3	37.8	0.36	94.3	0.188
5A	37	0-0-0	170/100	Neg.	35	57	428	653	73.7	26.8	0.17	123.0	0.309
6A	62	0-0-0	240/130	Neg.	41	100	440	750	59.8	29.7	0.13	97.9	0.221
7A	51	0-0-0	170/95	Neg.	45	108	560	1010	63.7	30.8	0.23	118.0	0.218
8A	37	0-0-0	230/130	Neg.	37	87	365	580	57.8	21.8	0.19	100.0	0.239
9A	48	0-0-0	150/95	Neg.	41	60	445	745	58.2	19.4	0.24	0.23	
10A	50	0-0-0	160/100	Neg.	40	64	327	550	71.1	33.7	0.17	0.26	
Total average			185/110		39	82.8	409.1	675.8	58.0	23.0	0.216	96.7	0.236



TABLE II. CLINICAL DATA AND TABULATION OF CLEARANCE VALUES ON PATIENTS WITH HYPERTENSION. ALL PATIENTS HAD SUSTAINED A PREGNANCY COMPLICATED BY HYPERTENSION AND ALBUMINURIA

PATIENT	AGE	PARITY	BLOOD PRESSURE	YEAR OF TOXEMIC PREGNANCY	HEMATOCRIT	INULIN CLEARANCE C.C./MIN.	DIODRAST CLEARANCE C.C./MIN.	RENAL BLOOD FLOW C.C./MIN.	UREA CLEARANCE C.C./MIN.	URIC ACID CLEARANCE C.C./MIN.	FILTRATION FRACTION	UREA F.F. 0.60												
1B	61	5-3-2	230/120	1903, 1905	40	93	81	102	560	530	618	930	885	1030	61.0	28.0	26.0	26.0	0.16	0.15	0.17	100.0	0.178	
2B	55	2-0-2	160/110	1909, 1911	38	96	85	82	492	465	435	792	750	700	68.8	63.0	45.0	42.2	0.18	0.19	0.195	111.0	0.239	
3B	43	4-2-2	180/110	1916, 1919	40	70	75	73	390	475	375	650	780	625	61.9	61.9			0.18	0.16	0.19	106.7	0.217	
4B	33	3-0-3	160/100	1931, 1938	40	95	85	92	347	328	348	580	492	580	68.7	65.3	36.7	32.2	0.28	0.26	0.26	107.3	0.314	
5B	37	5-1-3	160/100	1939	37	53	52	71	405	372		655	600		56.0	42.3	67.1		0.13	0.19		112.0	0.289	
6B	33	1-0-1	145/90	1940	35	93	82	470	465	438		720	660		79.2	76.2	37.5	33.3	0.21	0.19		128.0	0.282	
7B	23	1-0-0	144/94	1941	46	75	84	388	365	210		690	650	550	58.0	63.0	22.0	18.0	0.19	0.23		100.0	0.282	
8B	33	2-0-1	135/90	1941	40	119	100	290	330			485	550		61.0	55.3			0.41	0.30		-	-	
9B	34	3-1-1	140/90	1941	34	76	84	472	450	460		715	680		61.0	55.3			0.16	0.19		185.0	0.346	
10B	28	1-0-1	150/100	1941	38	128	123	119	580	530	495	935	854	798	119.8	114.3			0.22	0.23	0.24	168.3	0.497	
11B	23	1-0-1	120/90	1941	32	101	131	344	333			510	490		91.6	112.9			0.29	0.39		133.3	0.308	
12B	43	7-5-0	150/110	1941	40	86	74	73	430	428	380	716	714	670	77.1	83.4			0.20	0.17	0.19	183.3	0.299	
13B	34	2-1-1	150/90	1941	40	144	123	142	610	606	625	1020	1020	1030	103.5	106.9	30.7		0.24	0.20	0.23	126.1	0.290	
Total			157/100			93.0			434.5			720.8			75.7					0.217				

fraction while that of the nulliparous women parallels the inulin clearance closely. We are unable to explain this difference, but it seems likely that it is due to decreased resorption of urea.

In the toxemias of pregnancy and in the posttoxic hypertensives, several workers<sup>12, 18</sup> have postulated the existence of efferent arteriolar constriction added to a thickening of the glomerular membrane to permit a reduced glomerular filtration and control of the renal blood flow.

Smith<sup>1</sup> postulated the efferent arteriolar control of renal blood flow not because of the apparent increase in glomerular filtration, but because of the anatomic evidence of afferent arteriolar thickening in arteriolar disease<sup>19</sup> and the lack of demonstrable hypertension in the peripheral capillary bed of hypertensive patients,<sup>20</sup> it would seem likely that most of the control of renal flow and glomerular filtration is effected in the afferent arteriole.

Smith<sup>21</sup> has recently presented evidence that the reduced glomerular filtration rate in "toxemias of pregnancy" is found by using mannose as well as inulin and states that the difference in molecular size would argue against the thickening of the glomerular membrane as the etiologic factor. Lampert<sup>22</sup> has recently attempted to apply Poiseuille's law to the arterioles of the kidney and has been able to arrive at definite values for resistance in the afferent and efferent arterioles. We have applied his formula to our findings and have found that although significant increases can be found in the resistance of the efferent arteriole in hypertension (Table III), they are dwarfed by the changes in afferent resistance by even minimal increases in mean systemic blood pressure.

TABLE III. CALCULATED RESISTANCE IN THE AFFERENT AND EFFERENT ARTERIOLES IN THE POSTTOXEMIC HYPERTENSIVE AND THE NULLIPAROUS HYPERTENSIVE

	MEAN BLOOD PRES- SURE	INULIN CLEAR- ANCE C.C./MIN.	DIO- DRAST CLEAR- ANCE C.C./MIN.	RENAL BLOOD FLOW C.C./MIN.	RESIST- ANCE OF AF- FERENT ARTE- RIOLES (R. A.)*	RESIST- ANCE OF EF- FERENT ARTE- RIOLES (R. E.)*	TOTAL RESIST- ANCE (R.)	R.A./R.E.*
Hyperten- sion	147	82.8	404.1	675.8	99.1	32.1	131.2	2.08
Posttoxic hyperten- sion	123	93.0	434.5	720.8	67.3	30.1	97.4	2.23
Normal	100	120.0	600.0	1020.0	19.5	14.4	33.9	1.35

$$*R. E. = \frac{(1 - 0.47F)(Po' - 16.4)}{HD}$$

$$R. A. = \frac{Pm - Po' - 40}{HD}$$

HD, Renal blood flow

Po', Osmotic pressure of plasma

Pm, Mean systemic blood pressure

F, Filtration fraction:  $\frac{\text{Inulin clearance}}{\text{Diodrast clearance}}$

These results and previous findings in nonhypertensive posttoxic patients would tend to produce evidence that the changes in caliber of

the renal blood vessels are initiated by the hypertension, and that the causative agent of the elevated pressure (reduction of renal pulse pressure?) is the primary factor in this disease.

#### CONCLUSIONS

No evidence is found to support the theory that posttoxemic hypertension varies from hypertension in the nulliparous female.

Substitution of inulin for urea clearances in the determination of glomerular filtration shows no significant difference in glomerular filtration in the posttoxemic women when compared to those who have had no pregnancies.

Our data show that afferent arteriolar constriction plays a pronounced part in the regulation of renal blood flow in hypertension and suggests that the functional status of this arteriole may well explain most of the alteration of renal function found in this disease.

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## POSTERIOR ROTATION OF THE OCCIPUT DURING LABOR

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ON THE maternity service of the Hospital of the University of Pennsylvania, 96 parturient women were observed in whom posterior rotation of the occiput occurred during the course of labor. In about three-fourths of these patients, the infant was born spontaneously, face-to-pubis. Since this outcome was not expected, we decided to study these women as a special group. We wanted to evaluate some of the factors reputed to bring about posterior rotation of the occiput, and to determine whether any special risk was associated with this variation in the labor mechanism.

### MATERIAL AND METHODS

The patients were selected from the Ward Service during the five-year period from 1936 to 1940, inclusive. Special study was limited to those women who exhibited vulvar crowning of the fetal head with the face-to-pubis. To simplify the analysis further, deliveries of twins, and those of infants under 2,500 Gm. were studied separately.

The bony pelvis of the women selected were examined roentgenographically. Pelvic variations were described after the manner of Caldwell, Moloy, and D'Esopo.<sup>1</sup> Mensuration of pelvic dimensions was carried out according to the method of Ball.<sup>2</sup> In addition to the data obtained from the roentgenograms, the clinical records of these patients were compared with those of control clinic groups. No new mode of comparison was attempted. Instead, the investigation was centered on factors commonly mentioned in current textbook discussions of this subject.<sup>3, 4</sup>

### RESULTS

*Frequency.*—During the period covered by the study, 4,164 women were delivered vaginally of single-fetus, term pregnancies. Posterior rotation of the occiput was exhibited by 96 of these patients, an incidence of 2.3 per cent (Table I). The occiput rotated posteriorly from a primary posterior position in 87 patients, and from an occipitotransverse position in 9 women. No instance of posterior rotation was observed to follow occipitoanterior engagement of the fetal head.

Unfortunately, the true incidence of occipitoposterior position at the time of engagement could not be reported from our material, because many of the patients were far advanced in labor when admitted to the hospital. However, if the combined data of Danforth,<sup>5</sup> Caldwell, Moloy, and D'Esopo,<sup>6</sup> and Calkins<sup>7</sup> can be applied to our patients, about 1,041, or 25 per cent, had occipitoposterior positions of engagement. Only 87 of these women were known to exhibit posterior rotation, or about 1 out of every 12 patients.

TABLE I. THE INCIDENCE OF POSTERIOR ROTATION OF THE OCCIPUT (SINGLE-FETUS, TERM PREGNANCIES)

Total vaginal deliveries	4,164	
Primary occipitoposterior positions*	1,041	25.0%
Posterior rotations of the occiput	96	2.3%

\*The estimate of the number of primary occipitoposterior positions occurring in our patients was based on the assumption that the normal distribution, as calculated from the combined data of Danforth,<sup>5</sup> Caldwell, Moloy, and D'Esopo,<sup>6</sup> and Calkins,<sup>7</sup> was applicable to our clinical material.

*Fetal Size.*—The relation of infant size to posterior rotation of the occiput was analyzed first by investigation of the mean birth weight of term infants. It may be noted (Table II) that the infants of the women of the special study group were 110 Gm. heavier on the average than the babies of all clinic patients delivered during the same period. One patient delivered spontaneously, face-to-pubis, an infant weighing 4,730 Gm.

The second method of analysis was based upon the frequency of posterior rotation of the occiput in premature labors. In the 310 patients who delivered viable infants under 2,500 Gm., the incidence was 2.3 per cent. This frequency was identical with that noted in term deliveries (Table III).

*Parity.*—The parity of women who exhibited posterior rotation of the occiput was compared with the parity of all clinic patients delivered during the period of study. The incidence of nulliparity in the special study group was not significantly lower than the clinic average (Table IV). No correlation could be established between parity and fetal birth weight.

TABLE II. THE RELATION OF FETAL SIZE TO POSTERIOR ROTATION OF THE OCCIPUT

TERM, VAGINAL DELIVERIES	AVERAGE BIRTH WEIGHT OF INFANTS IN GRAMS
All patients (4,164)	3,310
Patients with posterior rotations (96)	3,420

TABLE III. THE RELATION OF FETAL MATURITY TO POSTERIOR ROTATION OF THE OCCIPUT

MATURITY OF THE FETUS AT DELIVERY	FREQUENCY OF POSTERIOR ROTATION PER CENT
Term (4,164)	2.3
Premature (310)	2.3

TABLE IV. THE RELATION OF PARITY TO POSTERIOR ROTATION OF THE OCCIPUT

TERM, VAGINAL DELIVERIES	FREQUENCY OF NULLIPARITY PER CENT
All patients (4,164)	27.5
Patients with posterior rotations (96)	25.3

*Size of Maternal Pelvis.*—The mean pelvic dimensions of the special study group were obtained from roentgenographic films and arranged according to pelvic plane. Since no measurements of a control group were available from our clinic, it was assumed that the data collected



by Thoms<sup>8</sup> from 200 normal women could be used for comparison. As can be seen in Table V, there was surprising similarity in the dimensions of each level of the birth canal. No evidence existed of pelvic contraction at the inlet, midpelvic, or outlet planes. The difference in length of the mean true conjugate diameters probably would not be significant statistically. However, the greater depth of the posterior segment of the inlet of women who exhibited posterior rotation may be a true variation from the normal.

*Shape of Maternal Pelvis.*—The various bony pelvic configurations of our patients were noted in Table VI. For comparison, we have recorded the distribution of pelvic types in a control group of 215 normal patients studied by Caldwell, Moloy, and D'Esopo.<sup>9</sup> It will be seen that a considerably higher than normal proportion of anthropoid pelvises occurred among patients exhibiting posterior rotation of the occiput. As Thoms<sup>10</sup> has noted in women with posterior positions, the principal inlet configuration observed in the study group consisted of a deep fore-pelvis with a narrow angle, and a rounded posterior segment. We failed to find android posterior segments except in combination with deep anthropoid forepelves. The few android pelvises noted otherwise had a rounded posterior segment. Even the flat pelvises were large and displayed sufficient backward sacral displacement to feature the capacious posterior space at midplane and lower pelvic levels which was common to this group. Two patients with minor grades of asymmetry of the

TABLE V. THE RELATION OF MATERNAL PELVIC SIZE TO POSTERIOR ROTATION OF THE OCCIPUT

AVERAGE PELVIC DIMENSIONS*	POSTERIOR ROTATIONS (96) CM.	CONTROL GROUP† (200) CM.
Inlet:		
Anteroposterior	11.9	11.6
Posterior sagittal	4.9	4.4
Transverse	12.3	12.3
Midplane:		
Anteroposterior	12.5	12.3
Transverse	10.3	10.2
Outlet:		
Transverse	9.1	9.1

\*All dimensions obtained from roentgenograms of the pelvis.

†Data of Thoms.<sup>8</sup>

TABLE VI. THE RELATION OF MATERNAL PELVIC SHAPE TO POSTERIOR ROTATION OF THE OCCIPUT

TYPE OF PELVIS*	POSTERIOR ROTATIONS (96) PER CENT	CONTROL GROUP† (215) PER CENT
Anthropoid	70.8	26.4
Gynecoid	17.7	39.5
Platypelloid	5.2	6.3
Android	4.2	27.8
Asymmetrical	2.1	—

\*Pelvises of mixed type were classified according to their predominant features, i.e. anthropogynecoid, and androanthropoid pelvises were collected in the anthropoid group, androgynecoid pelvises in the android group, and all flat types in the platypelloid division. The gynecoid group included pelvises with only minor variants from the pure form.

†Data of Caldwell, Moloy, and D'Esopo.<sup>9</sup>

forepelvis presented the only examples of pelvic deformity. No significant correlation could be established between the occurrence of posterior rotation of the occiput and the shape of the sacrum, number of sacral segments, or inclination of the plane of the pelvic inlet.

In order to test the frequency of posterior rotation in the various types of maternal pelvis, we have utilized the combined data of Caldwell, Moloy, and D'Esopo,<sup>9</sup> Rappaport and Scadron,<sup>11</sup> and Steele, Wing and McLane<sup>12</sup> to estimate the total number of pelvis of each type that might be expected to have occurred in our total 4,164 patients. Then, we have listed the known frequency with which each type of normal pelvis was observed in the 94 patients showing posterior rotation of the occiput (Table VII). Note that even in the anthropoid group, the frequency of posterior rotation was only 6.5 per cent. This low incidence can be accounted for, in part, by the reasonable assumption that about two-thirds of the 1,041 patients with anthropoid pelvis presented anterior or transverse positions of engagement of the fetal head. However, primary occipitoposterior positions probably occurred in one-third of this group,<sup>6</sup> or in about 345 women. Of these, only 68 patients, or 1 out of every 5, really exhibited posterior rotation.

TABLE VII. THE FREQUENCY OF POSTERIOR ROTATION OF THE OCCIPUT IN VARIOUS TYPES OF MATERNAL PELVES

PELVES		THE OBSERVED FREQUENCY OF POSTERIOR ROTATION	
TYPE	ESTIMATED NUMBER AMONG 4,164 PATIENTS*	NUMBER PATIENTS	PER CENT
Anthropoid	1,041	68	6.5
Gynecoid	1,999	17	0.9
Platypelloid	291	5	1.7
Android	833	4	0.5

\*The estimate of the distribution of each type of pelvis among our 4,164 parturient women was based upon the assumption that the normal distribution, as calculated from the combined data of Caldwell, Moloy, and D'Esopo,<sup>9</sup> Rappaport and Scadron,<sup>11</sup> and Steele, Wing, and McLane,<sup>12</sup> was applicable to our clinical material.

*Repetition of Posterior Rotation.*—The 72 multiparous women of the study group have given birth to 306 infants. Since nearly half of these babies were born in other hospitals, or in the homes of the patients, the position of the occiput at the time of delivery could not be determined in a significant number. However, 13 of the 72 multiparas were known to have exhibited posterior rotation of the occiput in two or more labors. It may be noted that 11 of these 13 women have exhibited anterior rotation in another labor. Separate analysis made of the roentgenograms and clinical records of these 13 women did not reveal any significant variation in fetal size, pelvic size, nor pelvic shape.

*Delivery.*—The mode of delivery of the 96 patients with posterior rotation of the occiput was shown in Table VIII. Note that 78 women delivered spontaneously, face-to-pubis, whereas 17 patients required the assistance of outlet forceps. In only 1 patient was the Scanzoni maneuver utilized. In spite of the low operative incidence, labor was not unduly prolonged (Table IX).

*Maternal and Infantile Morbidity.*—The morbidity observed among the patients and their infants in the study group was compared with

TABLE VIII. THE MODE OF DELIVERY OF 96 PATIENTS WITH POSTERIOR ROTATION OF THE OCCIPUT

DELIVERY	PATIENTS
Face-to-pubis:	
Spontaneous	78
Low forceps extraction	17
After rotation of the head:	
With forceps	1

TABLE IX. THE AVERAGE DURATION OF LABOR IN PATIENTS WITH POSTERIOR ROTATION OF THE OCCIPUT

TYPE OF DELIVERY	NULLIPARA		MULTIPARA	
	FIRST STAGE HOURS	SECOND STAGE HOURS	FIRST STAGE HOURS	SECOND STAGE HOURS
Spontaneous deliveries (78)	16.5	2.3	7.9	0.8
All deliveries (96)	18.5	2.8	8.1	1.0

TABLE X. THE MORBIDITY OF DELIVERY IN PATIENTS EXHIBITING POSTERIOR ROTATION OF THE OCCIPUT

MORBIDITY	POSTERIOR ROTATIONS (96)	CONTROL GROUP* (4,164)
	PER CENT	PER CENT
Maternal mortality rate	0.0	0.1
Infant mortality rate	0.0	2.7
Operative delivery rate	18.8	8.5
Lacerations and injuries:		
Second-degree tears	13.5	10.0
Third-degree tears	2.0	0.5
Febrile morbidity rate	12.5	11.6

\*All women delivered vaginally of term infants in the University Hospital during the period of the study.

that of all patients of the clinic who were delivered of term infants during the same period. It will be noted in Table X, that the only significant morbidity ascribable to the condition, or to the accompanying operative maneuvers was a slightly increased incidence of injury to the perineum.

#### DISCUSSION

Current textbooks of obstetrics<sup>3, 4</sup> list causes of posterior rotation of the occiput which often seem to lack foundation in fact. Thus, emphasis has been placed on the importance of the fetal head being too small to engage those forces of labor presumed to bring about anterior rotation.<sup>3</sup> However, aside from the observations by Plass<sup>13</sup> on a small number of premature infants, very little factual data have been offered to substantiate this point of view. Dawson,<sup>14</sup> on the contrary, has noted that the average birth weight of infants delivered face-to-pubis was about the same as that of babies born with the occiput anterior. Our data lend support to Dawson's observation, and indicate that fetal size can hardly be a significant factor in posterior rotation of the occiput.

It has been taught that a badly relaxed, or torn muscular pelvic floor of the mother may be responsible for failure of anterior rotation of the occiput.<sup>3</sup> This idea, which probably originated with Dubois,<sup>15</sup> lacks confirmatory data. Dawson<sup>14</sup> was unable to correlate posterior rotation of the occiput with multiparity. Our observations agree with his, and make it seem unlikely that the muscular pelvic floor plays a significant role in this mechanism.

Attention has been directed to the relation between the bony pelvis and the occipitoposterior position. Certain authors<sup>16, 17</sup> have referred to the importance of pelvic contraction in the etiology of this variation in the labor mechanism. On the other hand, Fabre and Trillat,<sup>18</sup> Thoms,<sup>10</sup> and Hastings and Young<sup>19</sup> have reported that the anteroposterior dimensions of the pelves of these patients were increased. In the present study, wherein the problem of disproportion was eliminated by the method of selection of patients, the dimensions of the pelves were within the limits of normal variation. As Thoms,<sup>10</sup> and Caldwell, Moloy, and D'Esopo<sup>20</sup> have noted previously, the anthropoid inlet configuration with ample posterior space at lower pelvic planes was observed. We were unable to confirm the report of Hanson<sup>21</sup> that transverse midpelvic contraction was a significant variation in patients with persistent occipitoposterior positions.

The frequency of the anthropoid pelvic shape in parturient women exhibiting posterior rotation of the occiput should not lead to the conclusion that a high incidence of face-to-pubis delivery may be expected in anthropoid pelves in general. In addition to this shape of pelvic inlet, ample anteroposterior space must be available at lower pelvic levels and the fetal head should have begun descent into the pelvis with the occiput posterior. Even when this combination of factors is operating, the probability of face-to-pubis delivery is only about 1:5. It would appear, therefore, that there has been a failure to work out other factors predisposing to posterior rotation. Study of deflexion attitudes of the head, shape of the fetal head, position of the placenta, and axis of the cervix may give additional information.

The classification of posterior rotation of the occiput as an anomaly of the mechanism of labor seems to be based mainly on the infrequency of its occurrence. The clinical results obtained in our patients, and in those of Dawson,<sup>14</sup> raise doubt of pathologic significance. Additional maternal effort was required for spontaneous delivery, and the perineal stage did not progress with quite the same ease observed in anterior positions of the occiput. However, no harm to mother or child attended the outcome when complete posterior rotation of the occiput was exhibited. We hasten to add that these remarks should not be construed to refer to midpelvic "arrests" with the occiput posterior. Incomplete rotation of the occiput in a posterior, or any other position, introduces factors beyond the scope of this presentation.

## SUMMARY

1. Posterior rotation of the occiput was observed in 96 of the 4,164 patients who were delivered vaginally of term infants.

2. Posterior rotation of the occiput was exhibited by one patient out of every twelve who presented occipitoposterior engagement of the fetal head. It was not noted after primary occipitoanterior positions, and only rarely after transverse engagement.

3. No etiologic significance could be attributed to small fetal size, relaxation of maternal soft tissues, nor gross pelvic deformity.

4. The mean dimensions of the bony pelvis of patients of the study group were only slightly different from those of a control group of women. A trend was noted toward anteroposterior spaciousness at all pelvic levels.

5. A high incidence of anthropoid pelvis was observed in the par-turient women studied. Android pelvic types were seen rarely.

6. Posterior engagement of the occiput in an anthropoid pelvis introduced a probability of complete posterior rotation in one out of five patients.

7. No special pathologic significance could be attached to this variation in the labor mechanism.

I wish to express my appreciation to Dr. Carl Bachman for guidance in this study.

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## SPONTANEOUS ABORTION AND ITS TREATMENT WITH PROGESTERONE

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THE age-old controversy as to whether heredity or environment plays the greater role in human development is not confined to the post-partum period of life, but involves intrauterine life as well, and the gametes, themselves, in a consideration of the cause of spontaneous abortion. Particularly is this true in those cases without obvious cause. Upon careful study, causes are sometimes found which are not obvious, such as hypothyroidism, for example.

The work of many able observers has established beyond any doubt that many of these early abortuses are pathologic, from 50 to 80 per cent, according to different workers. Mall<sup>1</sup> has divided pathologic ova into seven groups, from those showing villi only to a chorion and amnion containing a macerated embryo. Normal embryos were those in which the embryos were normal or possessing only localized anomalies. Hertig and Edmonds<sup>2</sup> found pathologic ova in 47.4 per cent of 53 consecutive cases of spontaneous abortion, and in these hydatidiform degeneration was found in 66 per cent. The mean duration of the pregnancy in these cases was ten and two-tenths weeks, which is in agreement with clinical experience that most spontaneous abortions occur between the second and third months.

The difference of opinion begins when an attempt is made to account for the pathologic abortuses. These opinions fall into two divisions: (1) that abnormalities in the germ cells themselves are responsible for the pathologic ova or embryos, and (2) that the observed pathologic abortuses are due to abnormalities in the maternal developmental environment.

Mall,<sup>1</sup> after an exhaustive study of abortuses, expressed it as his belief that all of these abnormalities, from the least to the greatest, were due to faulty implantation. He says, "In my paper on monsters, I stated that on account of faulty implantation of the chorion, the nutrition of the embryo is affected so that if the ovum is very young the entire embryo is soon destroyed, leaving only the umbilical vessels within the chorion, and this also soon disintegrates, leaving only the chorionic membrane, which in turn collapses, breaks down and finally disappears entirely. . . . I have attempted to point out that the primary cause is in the environment of the egg, and that the arrested development is associated with destruction of tissue."

Meyer<sup>3</sup> on the other hand does not agree. He says, "Although we know very little about the existence of abnormal ova, the relative fre-

quency with which anomalous forms of spermatozoa occur would alone seem to make decidedly venturesome the assumption that there is no such thing as germinal anomalies. In view of the fact that we frankly recognize the occurrence of hereditary anomalies, germinal causes certainly can not be excluded. . . . It is strange that we know so little regarding the anomalous development of the chorion as a factor in the termination of pregnancy. That the cause for the latter not infrequently may be sought in the ovum or spermatozoon one can scarcely doubt, for otherwise one would have to assume that the human reproductive cells are characterized by a unique immunity and perfection."

Corner,<sup>4</sup> in a careful study of the reproductive processes in swine, states, "The question of embryonic pathology in mammals appears less simple the more we learn of the complex factors which control normal development of the embryo. Appearance of a dead or malformed embryo is but the end result of maladjustment somewhere along the intricate mechanisms of fertilization and segmentation, transportation of the embryo through oviduct and uterus, the establishment of placental connections with the maternal organism and the nutrition of the growing embryo. We have not advanced far toward an analysis of these factors in the causation of embryonic mortality. In general, those who approach the question from the standpoint of human embryology lean toward the position of the late Professor Mall, who held that a defective maternal environment, usually in the nature of faulty implantation, is the chief source of morbidity in mammalian embryos, while the geneticists and those embryologists who are familiar with the earliest stages of mammalian development tend to believe that the embryo itself may be the subject of internal defects, which may be hereditary in character or at least may arise during the earliest stages of embryonic existence, or in the germ cells themselves. . . . Summing up these cases of pregnancy examined during the period of implantation, it seems that in the pig there is little evidence that faulty implantation is the cause of embryonic mortality and abnormality, but much to indicate that embryos may become abnormal in spite of a uterine environment which by all the criteria at our command is anatomically and functionally normal. . . . Yet it cannot be claimed that all maternal causes have been ruled out by the type of investigation we have been able to make, however refined the discrimination which we have applied in our microscopic studies. The proof of histological normality does not, for instance, rigidly exclude the possibility of chemical lesions proceeding from altered secretions in the Fallopian tubes and uterus, without visible cytologic change. It is even conceivable that nutritional disorder might alter the uterine environment without detectable change in the endometrium."

The trend has thus been away from environmental factors toward abnormalities in the germ cells themselves as the chief cause for spontaneous abortion. Lethal or sublethal factors, or defects in the genes of the chromosomes, have been found by geneticists in both vegetable and invertebrate material, a particularly exhaustive contribution having been made by Morgan and his co-workers in their investigations on the fruit fly, *Drosophila*. In this fly they have shown that certain combinations of genes in fertilization are incompatible with development of the ovum. Others may be sublethal, and result in defective embryos. Since

the human animal has not proved to be unique in any fundamental biologic particular from the rest of the animal kingdom, there is at present no basis for a belief that his germ cells are the one exception.

These two trends of opinion have a distinct bearing upon us as clinicians, when faced with the problem of abortion in the human being. Granting that from 50 to 80 per cent of all abortuses are pathologic, if we are convinced that these result primarily from defects in the germ cells themselves, then it is obvious that no treatment directed toward the mother, of any nature whatever, whether begun as soon as the pregnancy can be diagnosed or at the instant of a "threatened" abortion, can have any favorable influence. And since we know practically nothing regarding means to improve the germ cells per se, the picture becomes dark indeed.

However, clinical experience and the numerous reports in the literature during the past few years, concerned with the favorable results of treatment of abortion, even though they may be, as Paine<sup>5</sup> says "hardly more than testimonial evidence," must bear considerable weight in our evaluation of the advisability of such treatment. Clinical evaluation is most difficult and beset with many pitfalls, but it is not until enough cases are reported to be of statistical significance that a final judgment of the worth of any method of treatment can be made.

The incidence of spontaneous abortion has been estimated variously by different writers and investigators.

Williams (in 1917) was of the opinion that it was at least one in every five or six pregnancies. Meyer estimated that out of every 100 fertilized ova, only 78 develop to term, the rest being aborted. Taussig,<sup>6</sup> quoting Dr. Kopp's book *Birth Control in Practice*, gives something over 8 per cent of spontaneous abortions in 38,985 pregnancies. In addition, there were 69 per cent of induced abortions, and since it is obvious that a considerable number in this class would have aborted spontaneously if induction had not occurred before this could happen, it is evident that the incidence of spontaneous abortion in this large number of pregnancies would probably have been considerably in excess of 8 per cent.

#### PERSONAL OBSERVATIONS

The following report on the treatment of abortion is based upon a series of 311 consecutive pregnancies, all of which were cared for by me personally in private practice. In these 311 pregnancies, there were a total of 19 abortions, or an incidence roughly of 6 per cent. Six of these abortions were in two patients, who had three each. Some of these cases aborted without treatment and some represent failures in treatment. They are included without differentiation at this point.

This incidence of spontaneous abortion is considerably less than is generally reported. However, all of these women were in comfortable circumstances of life. Almost without exception, they reported early for prenatal care. Adequate diets were insured, with particular attention to proper intake of calcium and other minerals, and vitamins.

Thyroid extract or iodine, as indicated, was frequently given on the basis of either a basal metabolism test or history. Foci of infection were cared for as soon as possible.

If from 50 to 80 per cent of abortuses are pathologic and if the chief cause is defects in the germ plasm, then no somatic factors affecting the mother should make any difference. Few diseases, of whatever severity or chronicity, seem to affect the germ cells themselves, or the fertility of men or women. We know that thousands of women lose their lives yearly because of this fact. If, on the other hand, the maternal environment is a major factor in abortion, all of the factors incident to a comfortable life, as well as treatment directed to the prevention of abortion, ought to make considerable difference. The fact of a low abortion rate in a series of women of this class, together with an apparent considerable success in the treatment of abortion in these women, the fertilized ovum being a fait accompli, would seem to lend confirmatory evidence to the latter view.

In this series of 311 pregnancies, there were 34 "threatened" abortions which were treated. These were manifested by painful rhythmical uterine contractions, or bleeding, or both. In 30, or 82 per cent, the abortion did not occur and the patients were carried to term. Four aborted in spite of treatment. One of these was carried to term in her next pregnancy by prophylactic treatment begun shortly after the first missed menstrual period. The other three were lost sight of.

In addition there were 17 patients who were treated prophylactically from the beginning of their pregnancies. These patients gave a history of having had from one to three previous consecutive abortions, and several of these had been preceded by long periods of sterility before the first pregnancy, or between abortions.

Of these 17 patients, 15 were carried to term the first time such prophylactic treatment was given. All gave birth to entirely normal babies, who continued to develop normally thereafter. This represents a success of 88 per cent in this group of patients, which contained those with a most unfavorable previous reproductive history.

The two failures in this group are the same two who figured in six of the total number of abortions (19) mentioned above, and leaving aside the three patients previously referred to, whom I did not see subsequent to their abortions as primiparas, represent the only two patients in the entire series who were not carried to term, to be delivered of normal babies, either when treated the first time for "threatened" abortion, or the next time, when prophylactic treatment was instituted upon the diagnosis of pregnancy.

In addition to all other measures which should constitute good prenatal care, which have been previously mentioned, the only other agent which was used in the treatment of "threatened" abortion, or in the prophylactic treatment of abortion, was progesterone (poluton, Schering). In no case was morphine used. It is my opinion that morphine has no place in the preventive treatment of abortion and should be used only for pain in inevitable abortion. This opinion is based upon clinical



experience with it, and experimental evidence by those who have shown its action upon the gravid uterus.

Progesterone was used in 5 mg. doses (intramuscularly in oil) in cases of threatened abortion. If the symptoms were slight, being marked only by slight cramping or slight bleeding or sometimes both, this dose was given once daily. One injection usually resulted in a disappearance of pain in the very early case. If the symptoms were more severe, 5 mg. were given twice daily, frequently for several days. As soon as cramps and/or bleeding ceased, the progesterone was not immediately discontinued. Usually 5 mg. were given every other day for several days. The dose was then reduced with the same interval to 2 mg. This was continued for a week or more, then the intervals lengthened and injections continued for perhaps two more weeks. Unless cramps and/or bleeding were moderate, these patients were not kept at strict bed rest, but came to the office for treatments. Twelve of the patients were hospitalized, not so much for strict bed rest as for the convenience of giving the injections more than once a day, and to have them there if treatment was unsuccessful. I believe that these early spontaneous abortions are definitely upon an endocrine basis, and that normal physical activity has little to do with them, one way or the other.

In those patients with a recurrent abortion history and who were treated prophylactically, progesterone therapy was begun as soon as the diagnosis of pregnancy could be established. Sometimes this was clinically, and sometimes on the basis of a positive Friedman or Aschheim-Zondek test.

If the patient had had two previous abortions, and no successful pregnancy, she was usually given 5 mg. of progesterone three times a week, and that amount daily through the second and third missed menstrual period times. If possible, 5 mg. doses were continued three times weekly through the fourth missed period, then reduced to 2 mg. three times a week. After the fifth month it was given twice a week through the seventh month, when it was usually stopped, although in three cases it was continued beyond this time.

In several instances, in spite of prophylactic treatment as indicated above, there were beginning cramps and/or bleeding at the time these abortions generally occur, viz., between the second and third months. When this happened, the patient was put to bed, one of the barbiturates given, and the frequency of progesterone administration increased. In several instances this was given in 5 mg. doses every four hours for twenty-four hours. In all cases, except the two previously mentioned, whose records are summarized below, the pregnancies were carried to term, with the birth of normal babies.

CASE 1.—L. H., aged 22 years in 1938 when the first pregnancy occurred, had been married for almost four years, without conception. A



sterility study was done, with no apparent cause being found for the failure of conception, in either the husband or the wife. Basal metabolic rate was minus 3 per cent, and she was given thyroid extract. Conception followed tubal insufflation test, with one menstrual period intervening. Whether the thyroid or the insufflation had anything to do with this conception, I do not know.

Two and one-half months after the last menstrual period severe cramps began, together with some mbleeding. Five milligrams of progesterone were given. The cramps were markedly reduced in severity for about ten hours, when they recurred with a marked increase in the bleeding. At this time the abortion was considered inevitable and no further treatment was given, except morphine for pain. Abortion was complete in about two hours. No embryo was found in the material passed, and the pathologic report was only of placental tissue.

The next pregnancy was in January, 1940. This was treated prophylactically as outlined above. Bleeding began at the time of the second missed menstrual period, and in spite of increased doses of progesterone, abortion occurred within six hours. Pathologic examination of the abortus showed evidence of hydatidiform changes as described by other authors quoted herein.

The third pregnancy occurred in January, 1942. Prophylactic treatment was not given. Except for marked nausea and vomiting, which responded well to treatment, the pregnancy was uneventful until in March, nine weeks after the last menstruation, when bleeding began. Large doses of progesterone were given, but abortion was complete at ten hours. No embryo was found. This time the villi showed no evidence of hydatidiform changes.

CASE 2.—E. H. had been under treatment, for some time, by an internist for certain allergic manifestations, together with a marked hypothyroidism. She was considerably overweight, and there was a marked generalized hirsutism, especially on the face and neck. Other than this her general structure was typically feminine, as was her voice. Menstrual history was essentially normal.

The first pregnancy dated from May, 1939. Other than routine prenatal care, no treatment was given in this first pregnancy. In July, ten weeks after the last menstrual period, painless bleeding began. Large and frequent doses of progesterone were given, but the bleeding continued actively. Severe cramps began thirty-six hours later, and abortion was complete in twelve more hours.

The next pregnancy began in October, 1940. In addition to the usual prenatal care, she was placed on wheat germ oil and given 5 mg. of progesterone twice a week. This pregnancy was diagnosed early by the Friedman test. In spite of increased doses of progesterone, she aborted during a three-day period in December, 1940, nine weeks after the last menstrual period.

The third pregnancy dated from April, 1941. The usual measures in prophylactic treatment were taken, including vitamin E. The dose of progesterone was increased to 5 mg. three times a week, and daily through the second missed menstrual period. Ten days after this time, slight bleeding and some cramps occurred. She was hospitalized and 5 mg. of progesterone were given every four hours for twenty-four hours,

by which time the pain and bleeding had stopped. The progesterone was gradually reduced over the next several days, and the patient was about her accustomed duties a week later. There were no further signs or symptoms of abortion.

By September, the uterus had enlarged to a much greater extent than justified by the duration of pregnancy, and the fetus could not be definitely palpated, and it continued to grow rapidly over a period of the next three weeks. Diagnosis of polyhydramnios was made. An x-ray picture was made in October, at which time a diagnosis of an anencephalic fetus was reported.

Because of the history of two previous early abortions and the patient's intense desire to have a baby, the fact that fetal movements were daily felt, combined with the faint hope that we might all be wrong in our diagnoses, the pregnancy was not immediately terminated. However, one week later, contractions began, and on admission to the hospital the cervix was dilated about 4 cm. and the membranes were bulging through it. These were ruptured, with the escape of over 7 liters of fluid. Following this, contractions were strong and almost continuous until the delivery about three hours later of a stillborn anencephalic fetus of about seven months. There were also a complete spina bifida and many other skeletal abnormalities.

The uterus contracted well, the blood loss was minimal, and a grossly normal placenta was delivered, which did not show any essential histologic abnormality. Convalescence was uneventful.

Between this patient's second and third pregnancies, a diagnostic curettage was done at the beginning of a menstrual period, and the hyperplasia and secretory changes were excellent. Her thyroid rate had been maintained at a normal level for several years by treatment.

The percentages of success in these two classes of cases, viz., 82 per cent in the treatment of "threatened" abortion, and 88 per cent in the prophylactic treatment, agree closely with that reported by Falls<sup>5</sup> in his treatment of abortion by progesterone of 85 per cent success. As I have stated, clinical evaluation is difficult and I am fully aware that perhaps some of the patients in both of these classes would not have aborted, in spite of contractions or bleeding, or both, if nothing had been done. On the other hand, treatment, such as outlined, has resulted in success far greater than other methods of treatment which I have used in the past.

It is difficult, in the face of clinical results such as these and others which have been reported, to adopt the attitude of helplessness and hopelessness in the problem of spontaneous abortion which would be indicated by reading some of the literature, or particularly to desist in the preventive treatment of abortion through fear that even if successful, babies might be born that were better unborn.

We must agree that some abortions are doubtless due to inherent defects in the germ cells themselves and that these defects may be of a nature which does not permit survival of the ovum or embryo. In such cases it is doubtful if any treatment would result in their survival. Such a case may be represented by "L. H." above. Other defects in the

germ cells may exist which result in an embryo that may or may not develop to term in utero. Some of these might be aborted if let alone, and it might or might not be possible to prolong their existence, perhaps even to term, by intensive treatment. To do this would obviously be most unfortunate therapy. Case "E. H." above seems to be one of these.

If the views of those who believe that defects in the germ cells are the major cause of spontaneous abortion are correct, then one or the other of two conditions should follow. Either it should not be possible to carry many of those pregnancies to term, or if it is possible, then there should be a great many more abnormal babies born. The most encouraging note in this series of cases is that in not a single instance was a baby born at term that was not in every way normal. One of the abortions figuring in the total of 19 was represented by an hydatidiform mole, and another by the seven months' anencephalic fetus already described.

What the action of progesterone is in these early cases of spontaneous abortion, if it has any specific action, is difficult to say. The great majority of such abortions occur between the second and third months, at the time when placentation is occurring, and the influence of the corpus luteum of pregnancy is waning. I have thought that abortions at this time might be due to a too rapid regression of the corpus luteum, or a delay in the assumption of hormone function by the placenta, resulting in a lowering of the progesterone level below that necessary for a continuation of the pregnancy.<sup>9</sup> Falls and others<sup>7</sup> have reported a diminution or cessation of uterine motility following the administration of progesterone. Bickers,<sup>8</sup> by the same method, however, finds no effect upon the gravid uterus. It is impossible at the present time to reconcile these conflicting results.

We must agree with Paine<sup>5</sup> that what is needed most is some way to diagnose early the inevitable abortion, or the abortion resulting from an abnormal ovum, from those which are fortuitous and which might be prevented by proper treatment. Careful attention to history will frequently make it possible to treat abortion at the most favorable time always to treat it, viz., as soon afterwards as conception can be diagnosed, and many times preferably before conception.<sup>9</sup>

Until increasing knowledge clarifies the causation of spontaneous abortion, clinical experience emphatically justifies our continued efforts to prevent it, both by therapeutic and prophylactic treatment; howbeit in the light of our present knowledge, such efforts will frequently be predestined to failure, and in some cases to unnecessary or unwise treatment.

#### CONCLUSIONS

1. Spontaneous abortion may be due to defects inherent in the germ cells or to maternal environmental factors. Neither cause has been proved to the exclusion of the other. Probably both are concerned.

2. Results of good prenatal care, together with reported successes in the therapeutic and prophylactic treatment of abortion, lend some support to the latter of the causes mentioned above, and at least justify continued efforts in preventive treatment.

3. Progesterone appears to be a valuable adjunct in the treatment of spontaneous abortion.

Proluton was supplied by the Schering Corporation.

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1011 REPUBLIC BUILDING

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## USES AND ABUSES OF RADIATION THERAPY IN OBSTETRICS AND GYNECOLOGY\*

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IT WAS in the province of gynecology that radiation therapy was first used to any considerable extent, and in this field it is still one of the most important therapeutic agents. At first radium and x-rays were used almost entirely for the treatment of malignant diseases, because neoplastic growths presented focal aberrations of tissue growth which were tangible entities toward which the rays could be directed. Furthermore, such growths constituted so real a hazard to their hosts that the use of drastic and somewhat experimental therapeutic agents which might destroy them was a justifiable procedure. Experience has taught that not all malignant processes are amenable to such treatment and, moreover, that there are undesirable remote effects which must be taken into consideration. In the application of radiation therapy to gynecologic ailments, there is an increasing volume of advanced malignant disease in the treatment of which radiation is preferable to excisional surgery. In those instances where the malignant disease has passed beyond all help from surgical removal, radiation is frequently the best method of palliative treatment, but, even in these cases, we are finding that radiation must be used with discrimination. It is a misconception,

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however, to think of radiation therapy as a technique which may properly be used in the treatment only of malignant disease. As time passes, we learn of new uses in connection with benign conditions. A generation has passed since widespread therapeutic use has been made of radiation therapy, and, while many have evaluated the use of these agents from the point of view of a particular type or group of malignant diseases, there have been few efforts to assess the value of this form of treatment from the more general point of view.

In this consideration, we will not take into account misuses or bad results due to the employment of grossly improper dosages, inadequate filtering of the rays, or lack of diagnostic ability. In order that we may consider the problem on its intrinsic merits, we must assume that the technique of the therapy and the correctness of the diagnosis are satisfactory.

Since the indications for and against radiation therapy in gynecology and obstetrics are influenced considerably by the different phases of life in the woman, they should be regarded, to begin with, from an age period point of view and then evaluated with respect to the various clinical entities, both benign and malignant. The most convenient divisions of the life span for this purpose are:

- |                            |                              |
|----------------------------|------------------------------|
| 1. Pre- and postpuberal    | (First two decades)          |
| 2. Reproductive            | (Third and fourth decades)   |
| 3. Pre- and postmenopausal | (Fifth and Sixth decades)    |
| 4. Senescence              | (Seventh and eighth decades) |

#### PRE- AND POSTPUBERAL PERIOD (FIRST TWO DECADES)

The use of roentgen rays or of radium for the treatment of gynecologic dyscrasias in the first decade of life should be confined to the treatment of the rare instances of malignant disease. These are usually the embryonal types of epithelial or connective tissue tumors. Unfortunately, malignant tumors in the young are rarely diagnosed early enough or found in a sufficiently advantageous position to permit surgical excision. The occasional exception to this statement is the infrequently encountered malignant dysgerminoma. When this tumor is found, the indication is considered to be excisional surgery, aided by the use of x-rays or radium therapy. Although few persons have seen enough of these tumors to justify any very definite attitude toward their treatment, the consensus of opinion seems to be that they should receive radiation treatment. In addition, the granulosa cell tumor of the ovary should be mentioned as it is occasionally found in the first decade of life and is most often associated with precocious puberty. There has been much misconception concerning the significance of this growth, largely because it has been indiscriminately called "granulosa cell carcinoma," a term which, of course, implies malignant characteristics. This misleading nomenclature is unfortunate, for most granulosa cell tumors are benign, in fact, less than 20 per cent develop malignant characteristics. Radiation therapy, if it is to be used, must therefore be applied only to those patients from whom a granulosa tumor has been removed which has definitely malignant histologic features.



Even then there is some doubt, as will be shown later, whether radiation therapy has any thing to contribute.

In the second decade of life, the chief indications advanced for radiation therapy are the physiologic malfunctions of the hypophysis, the ovaries, or the uterus. These indications are most frequently represented by infantilism of the genital organs or as scanty, absent, or infrequent menses on the one hand, and excessive bleeding on the other.

From the point of view of the conservative gynecologist, radiation therapy can have little place in the treatment of malfunction of the menses at this period of life. The use of the so-called "stimulating dose" of x-ray or of radium directed toward the hypophysis, the ovaries or uterus must be considered an abuse, because there is almost complete lack of specific knowledge as to what constitutes a stimulating dose, if indeed there be such a thing, and because permanent harm may result, not only to the organs intended to be affected but also to other contiguous structures. Furthermore, the evidence that any permanent good can be expected to result from such treatments is not sufficiently substantiated to be at all convincing.

One hears much of the "temporary castrating" dose of radium or of x-rays. As this application of ray therapy has had fairly common usage, a great deal more is known about it than the so-called "stimulating dose." That the function of the ovaries can be suppressed through the effect of rays upon the Graafian follicle system has been well established. However, to secure this result without producing complete atrophy of the granulosa cells, the dosage must be most carefully graduated according to the age and the habitus of the patient, that is, the younger and thinner the patient, the lower the dose. The computation of the dose and the application of the treatment require great care and exact judgment. These prerequisites are so frequently lacking or are so subject to error that the method is often disappointing and therefore should seldom if ever be used. Indeed, other means of treating the ordinary causes of excessive postpuberal bleeding are so well known and with perseverance are so effectual in almost all cases that one must consider the use of radiation therapy as unnecessary, and more than that, as dangerous because it is fraught with the possibility of permanent infertility and even castration. Until this form of radiation therapy is characterized by a much more accurate knowledge of the dosage received by the ovaries and its effect upon them, both immediate and remote, this application of radium and x-ray should not be used except in very unusual circumstances. We have not felt that it was necessary to resort to its use in a single instance of postpuberal bleeding, always finding that there were adequate means which were less dangerous and more conservative for controlling blood loss.

To summarize, one may say that excepting in the rare instances of malignant disease of the genital tract, it is extremely seldom that a justifiable gynecologic indication for the therapeutic use of radiation therapy can be found in young women under twenty years of age. We should take an active stand in restraining the use of the so-called "stimulating" or "temporary castrating" doses of radium or x-ray as they are often ineffectual or may do permanent damage even when applied under good auspices.

#### THE REPRODUCTIVE PERIOD OF LIFE (THIRD AND FOURTH DECADES)

In dealing with the gynecologic patient of the reproductive age period, the physician must always form his judgments with regard to the use

of therapeutic agents being guided by a sensitive appreciation of the importance of preserving the procreative function. Any form of treatment directed toward the cure of an ill which, at the same time precludes the possibility of childbearing, can only be justified when the dangers inherent in the disease are of such a magnitude as to fully warrant castration. The interpretation of that phrase "fully warrant" is necessarily vague and will differ greatly in many minds, having different backgrounds of training, temperament, and modes of thought.

Approaching the diseases of the reproductive period of life in which radiation therapy may be applied from this point of view, it is at once apparent that aside from those of a malignant nature there can be no wide use for radium and x-ray until the end of the period is approached or actually reached.

The use of the "stimulating dose" of x-ray applied to the pelvic fields to overcome sterility has been urged by some, and a few series of apparently successful cases have been reported in the literature. However, such experiments, for such they are, are inadequately controlled so that one cannot state with any degree of assurance that the radiation therapy was of substantial benefit. There is no indication, either clinically or experimentally, that x-rays or radium ever exert a stimulating effect. Also, we are left in complete ignorance as to immediate and remote damage that may have been sustained by patients so treated. It is obvious, therefore, that this is not a form of therapy which in its present state can be more than very sceptically accepted by a wise profession.

We should also point out that the use of penetrating rays for therapeutic purposes has not been in vogue for a long enough time to permit a complete knowledge of their very remote effects. It is quite possible that succeeding generations begotten by patients who have received x-ray and radium therapy may reveal inherited deficiencies of the germ plasm as a result of that treatment. The basis for calling attention to this possibility lies in the experimental work which has been done on *drosophila*, mice, and guinea pigs, which demonstrates beyond a doubt that in these animals the effect of radiation may be transmitted and appear two, three, or even four generations later in the form of abnormal developments of the extremities, resulting in partial or complete absence of arms or legs or with clubbed feet, as well as occasional abnormal pigmentation of the skin surfaces.

The attitude toward "temporary castration" should, we believe, be the same in this as in the earlier periods of life, because it cannot be adequately controlled and hence should not be applied unless, when as at the end of the childbearing period, one may be willing to accept complete castration, should this be the inadvertent result. Under the latter circumstances, the full castration dose will usually be preferable to a lesser one if the indication is really adequate for the use of this therapeutic agent.

Endometriosis may be one of the exceptions to the foregoing statement. This benign disease occurs with some frequency in women twenty-five or more years of age. As is well known, it may and often does destroy fertility. The pathologic process is dependent upon and is promoted by ovarian hormones coming largely from the maturation of the Graafian follicle. In these patients one occasionally may be warranted, in an effort to suppress ovarian function for a period of several months, to remove or decrease the stimulating hormones and thus to induce re-

gression of the pathologic process. However, more often than not, the ovarian tissue already damaged by the endometrial cyst formations will lapse into permanent abeyance of function when treated with even small doses of x-ray or radium. The more specific approach with the scalpel is therefore to be preferred, at least in the initial stage of treatment. This is particularly true because laparotomy will usually be necessary to confirm the diagnosis, at which time appropriate excisions can be carried out. However, any remaining ovarian tissue, which should be left in the young woman whenever possible, will often produce enough hormone to allow the continued growth of the endometrial process. It may be, therefore, that as a sequel to the laparotomy one may elect to use radiation therapy rather than to resort to a second or third laparotomy. Under such circumstances, castration by radiation even in relatively young women may be a highly conservative procedure.

Similarly the use of castration in treatment of carcinoma of the breast in women of reproductive age may be warranted, as there is very good evidence that not only normal mammary duct and alveolar epithelium are stimulated to growth by the hormonal products of the ovary but that the malignant cells of the same origin may respond in a similar manner. This therefore constitutes another exception to the conservative attitude which is well indicated.

It has been found that therapeutic abortion may be induced in the early stages of pregnancy by means of x-ray radiation. A sufficient dose, when directed toward the site of implantation in the uterus, brings about degeneration of the trophoblastic ectoderm, followed by death of the fetus and subsequent expulsion of the product of conception. Use of the method has been urged by some enthusiasts, chiefly because they claim it to be devoid of blood loss and that the dangers of infection may be greatly reduced. However, abortion produced by x-ray is at best an awkward procedure, because the product of conception is retained in utero for some time after death, and the procedure seems to lack sufficient advantage over other more prompt methods to recommend its widespread use. But even more important is the inescapable danger of radiation effects upon the ovaries; this probability is sufficient to condemn the method unless simultaneous castration is desired, which will infrequently be the case.

When carcinoma of the cervix or of the ovaries coincides with pregnancy, as it does very occasionally, it is wise usually to evacuate the uterus before attempting to give radiation therapy. Adequate x-ray therapy for carcinoma will either kill the fetus in the early stages of pregnancy or produce serious malformation, because the direct beam as well as the scattering of the rays must necessarily affect large portions of the body of the fetus. Radium, on the other hand, may not do so because it may be more locally applied and because the dosage decreases rapidly with each successive centimeter that it is placed away from susceptible tissues.

The treatment of myomas by means of radium or x-rays has been widely used, so that the advantages and handicaps of the method can be fully evaluated. Those who have had wide experience in the use of radiation for this purpose lay down the following criteria which must be fulfilled if this means of treatment is to be carried out without undesirable complications:

1. The size of the growth must not be over 12 cm. in diameter.
2. The growth must be fairly symmetrical or globular in shape.

3. Pedunculated tumors cannot be safely treated, as they may undergo rapid degeneration due to precarious blood supply and produce adhesions, obstructions, etc.

4. Submucous tumors are contraindicated because of the dangers of becoming infected.

5. Rapidly growing tumors may be sarcomatous and this form of malignancy is notoriously resistant to radiation therapy.

6. There must be no inflammatory involvement of the adnexal organs.

7. Myomas undergoing degenerative changes are not suitable.

To the foregoing we should add that the tumor must produce symptoms such as bleeding or mechanical disturbances.

This, all will agree, is a rather formidable list of contraindications which in themselves, if present, would leave only a small number of suitable cases. But if in addition one asks how can one be sure that they are fulfilling these conditions, except by means of exploratory operation, it would seem at once to the trained surgeon that operative removal is by all odds the procedure of choice except in a few patients near the menopause with small and suitably placed tumors in whom ovarian conservation is not essential, or in patients who because of other diseases are not fit candidates for operation. In short, it would seem that there are only a very few instances of myomatous uterus that could not be treated better by surgical excision than by radiation.

The treatment of carcinoma of the cervix constitutes the greatest use which can be made of radiation during the reproductive period of life. That it has been a great aid and that it is the best mode of therapy in all stages of this disease, excepting the very earliest, is unquestionable. More will be said later on this subject.

#### PRE- AND POSTMENOPAUSAL PERIOD (FIFTH AND SIXTH DECADES)

As the menopause is approached, the desirability or possibility of childbearing having largely or completely passed, that is, in women forty or more years of age, the indications for the use of radium and x-ray in the treatment of benign conditions increase. Hyperplasia of the endometrium when it does not yield to curettage or hormonal treatment, endometriosis, the submucous myoma which produces excessive blood loss, and adenomyoma all may be treated efficiently and with the obviation of laparotomy by means of radiation. Here, contrary to the usage of many, x-ray may be preferable to radium. Intracavitary radium in 1,400 to 1,600 mg. hour doses is quicker and in many instances satisfactory. However, when there is danger of infection in the uterus or adnexal organs, and there frequently is such danger, the deep x-ray treatments are distinctly preferable. If the myomas are large enough to produce crowding of the pelvic organs and thus instigate pressure symptoms, it is very doubtful whether any form of radiation will prove a satisfactory solution. In these instances, even though the menopause, with its cessation of ovarian function and, hence with a recession of the growth stimulus, is imminent, and even though, as is well known, there may be and usually is a diminution in the size of the tumors, laparotomy with surgical excision of large tumors will nearly always prove to be the most satisfactory mode of attack.

The treatment of pruritus of the vulva and anal region should be mentioned, not only because of the frequency of these ailments at the



menopause and afterward, but to point out that the use of even the most superficial x-ray treatments to this region is not wise except perhaps in such small amounts as 75 r. for five treatments, for though they may give relief of the discomfort, they frequently are followed at a later time by abnormal skin changes closely analogous to kraurosis. This presumably is due to endarterial changes induced in the cutaneous capillaries which cause them to undergo gradual occlusion with consequent decrease in the blood supply.

#### THE USE OF RADIUM AND X-RAY IN THE TREATMENT OF MALIGNANT NEOPLASMS

Carcinoma of the vulva should never be treated by any form of radiation therapy, because doses sufficient to eradicate the cancer will result in fibrosis and other late manifestations which are undesirable. The perineum is notably the most intolerant skin surface of the body to radiation therapy. The only treatment is excision of the local lesion followed by dissection of the inguinal nodes. However, after operation, radiation of the inguinal region only has been recommended by some; on the other hand, many radiologists would advise against its use in this way.

From what has been said it is obvious that while radiation therapy has definite uses in nonmalignant states, it is with malignant conditions that its use should be chiefly concerned. This will remain true until the many undesirable side effects can be eliminated completely or at least minimized to a much greater extent than present techniques make possible. With cancer, however, it has proved to be a great boon to women when surgery is out of the question because of general debility, or when the neoplastic disease has advanced beyond the stage where excision is possible. This is true because cancerous processes in themselves constitute such an extreme hazard that the use of a drastic agent with its frequently undesirable side effects is indicated. There undoubtedly will be striking advances in techniques for the employment of the various forms of radiation therapy in the future as there have been in the past. As a result, the cure rate should be appreciably increased with a diminution in disadvantageous secondary effects. The past twenty years have seen notable advances in this direction. One of the most important recent improvements has been the application of deep x-rays directly to the cervix and parametria by means of the intravaginal cone. We have seen most encouraging regression following this technique.

Despite these real advances in radiation therapy and the others which may be forthcoming, there is urgent need for an entirely different approach to the problem of gynecologic cancer. Instead of waiting until the woman presents herself with the disease, the attitude of gynecologists should be one of aggressive prophylaxis. By that it is meant that we should obtain such a thorough follow-up of all women patients in the cancer-bearing period that we would thereby detect malignancy of the genital tract in its incipency when it can be treated and more frequently cured, not by radiation alone, but by a large variety of relatively simple and inexpensive means. This may sound somewhat Utopian, but much would be accomplished if every obstetrician and gynecologist applied the same general principles to the postreproductive care of women that are now in vogue during pregnancy and commonly



known as antenatal care. If semiannual physical examinations by competent gynecologists were available to cancer-susceptible women to the same degree that medical care is now available during pregnancy, we could, in a few years change the whole complexion of cancer therapy as far as the female generative tract is concerned.

This lack of constant and competent gynecologic observation of women in the cancer age constitutes the greatest omission of which our branch of the medical profession may be said to be guilty. This situation should be and, it is to be hoped, will be changed in the near future. An informed and well-trained staff of gynecologists should bring about the adequate training of physicians in sufficient numbers to make it possible to carry out such a program of cancer prophylaxis through semiannual examinations of women from the age of thirty-five to sixty or more years of age. Then and only then will we begin to meet the challenge of gynecologic cancer, because such observation is the only way in which the *early stages* of the disease may be detected.

#### RADIATION THERAPY IN THE AGED WITH ADVANCED STAGES OF MALIGNANCY

With what has seemed to be an increased incidence of advanced malignancy of all types occurring in women and with greater realization of the value of radiation therapy as contrasted to surgical treatment in the treatment of such patients, there has been an evergrowing tendency to refer all patients who are hopelessly ill with cancer to the roentgenologist for radiation treatment.

Sometimes marked regression of the malignant process results from treatment, or pain is greatly relieved. Thus the final days of the patient are not only made more comfortable but they may even be increased in number. (Such a result is not only desirable but it is the duty of the doctor to secure it for his patient if this is at all possible.) Unfortunately, however, the outcome is not always so fortuitous even under the best auspices. Frequently, instead of giving comfort and prolonged life, radiation produces nausea, vomiting, and added pain to such a degree as to constitute an augmented burden and make further life definitely less desirable to the patient. X-ray treatment of desperately ill or very aged patients with extensive metastatic disease is to be deplored with very few exceptions. It is much better, though the decision be a difficult one, to avoid the use of radiation in many such patients, because life under an increased burden of suffering may not be worth while if more discomfort is to be the lot of the patient. Furthermore, it is unfair to the radiologist to insist on radiation treatment only because the physician or the family are, so to speak, "grasping at last straws." The correct procedure should be to determine as accurately as may be possible the nature and extent of the malignant disease process, after which a consultation with the radiologist should take place in which the situation in the particular patient and in similar cases should be discussed, and the possible advantages and disadvantages thoroughly considered. Some patients will then be given radiation treatment carried out to an adequate degree to secure remission or palliation. Others, a border line group, will be treated tentatively with a trial of therapy to observe how the patient in general and the tumor specifically react to the treatment. If the response is found satisfactory, the treatment may be continued; on the other hand, when the response is poor the therapy should be stopped. Still other patients will

definitely be refused even palliative radiation treatment and will be given comforting drugs instead. In short, it is a great mistake to conclude that *all* patients with inoperable or recurrent cancer should receive radiation therapy, for often more harm than good is done.

Cancer of the cervix and that of the fundus of the uterus is well recognized and the various types are quite well differentiated (thanks to Martzloff, Schultz, and others who have devoted specific study to these lesions). In contrast, cancer of the ovary is not in such a well-ordered state of recognition, and therapeutics is discouraging, probably because the etiology and potential variations are much more complicated. Carcinoma of the ovary is a very common disease which, though varied in form and difficult to treat, should, we think, be accorded better therapy than it commonly receives. It is rather disappointing to read paper after paper on ovarian cancer coming, as many of them do, from good hospitals without anything like an adequate attempt at a critical analysis of the different histologic varieties of growth. The unqualified term, "ovarian carcinoma" means almost nothing beyond the mere fact that the process possesses the characteristics usually ascribed to malignant diseases. The life cycle of the different ovarian malignancies as well as their potentialities for harm are so varied as to require not only individualized consideration but widely divergent therapy.

A knowledge of the life cycle of the ovarian tumors and of their sensitiveness to radiation therapy is a definite prerequisite to the treatment of these lesions. Indeed, we need not confine this statement to ovarian neoplasms; it is equally true of all tumors of the female genital tract. Radiation treatment of the common forms of malignant neoplasm of the ovary, that is, the serous cystadenocarcinoma and the pseudomucinous cystadenocarcinoma, are most discouraging, particularly when the papillary processes have implanted themselves upon the serous lining of the abdomen and its viscera, if a cure of the disease is anticipated. However, deep x-ray therapy may and often does produce a temporary reduction in size of the tumor masses together with a decrease in the rate at which ascitic fluid is produced, so that the use of the deep x-ray may be helpful in making an inoperable tumor one which can be removed, as well as affording comfort to the patient for a period of months by diminishing abdominal distention due to ascitic fluid. On the other hand, cure by any means is rare.

#### SUMMARY

In conclusion, we may say that radiation therapy is very often a blessing, but it may also be a curse. Its use must be guided by clinical discretion and extensive knowledge of neoplastic and benign disease processes. The enthusiasm of radiation specialists is essential to the development of the art of radiation therapy; however, the application must be held within the bounds deemed suitable by conservative clinicians whose experience and long range point of view, in consultation with the radiologist, should dictate its use and decide upon appropriate application. In addition, let us again emphasize that the mere treatment of well-established or hopeless malignant processes by radiation and all other means is but to beg the question as far as the responsibilities and capabilities of the profession are concerned. Great ad-

vances will be realized when there is such a thorough and capable application of the prophylactic idea that we shall have the problem of treating genital cancer in its incipency rather than in its advanced stages. Such a program is not premature or in the least an unbridled phantasy; all that is lacking is a full appreciation by the profession of the simple methods by which such a program may be realized, and the zeal necessary for their appreciation.

## NUTRITION STUDY IN PREGNANCY\*

### FOOD HABITS OF 514 PREGNANT WOMEN

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THE food intake records of 514 pregnant women in Philadelphia were analyzed and recently reported.<sup>1</sup> The women represented several population, economic, racial, and nationality groups.

The diets, when compared with the recommended allowances of the National Research Council, were much below the standards for pregnancy. The average diet was 20 per cent below the allowance in calories, 22 per cent in protein, 53 per cent in calcium, 33 per cent in iron, 55 per cent in vitamin A, 43 per cent in vitamin B<sub>1</sub>, 47 per cent in ascorbic acid, and 50 per cent in riboflavin. Ten (2 per cent) diets could be termed good, 209 (41 per cent) fair, and 295 (57 per cent) poor. Calcium deficiency was the fault most constantly encountered.

When the food intake records were analyzed, no cognizance was taken of the specific foods which the women ate. A consideration of their food habits is the purpose of this report.

Weekly food consumption was compared with those amounts recommended for pregnant women in the pamphlet, *Planning Diets by the New Yardstick of Good Nutrition*, a publication of the Bureau of Home Economics. The weekly diet plans for pregnant women at three levels of cost, showing the food classifications, are shown in Table I.

### FINDINGS

**Milk.**—Milk makes many important contributions to the diet, the most notable of which is calcium. It also provides phosphorus, protein of good quality, vitamin A, thiamin, and riboflavin. It is a relatively cheap food and a wise purchase. Translated into servings, all three diet plans would indicate the daily use of at least one quart of milk to drink, in cooked food, or as cheese. Milk consumption in the group studied is shown in

\*This study was made under a grant from the Selina B. McIlhenny Fund for Clinical Investigation in the Presbyterian Hospital in Philadelphia.

TABLE I.\* KINDS AND APPROXIMATE QUANTITIES OF FOOD PER WEEK (FOR PREGNANT WOMEN)

	MILK† QT.	POTATOES, SWEET POTATOES LB.-OZ.	DRIED BEANS, PEAS, AND NUTS LB.-OZ.	TOMATOES, CITRUS FRUIT LB.-OZ.	LEAFY, GREEN, YELLOW VEGE- TABLES LB.-OZ.	OTHER VEGE- TABLES AND FRUIT LB.-OZ.	EGGS NO.	LEAN MEAT, POULTRY, FISH LB.-OZ.	FLOUR, CEREALS LB.-OZ.	FATS LB.-OZ.	SUGARS LB.-OZ.
Low-cost adequate	7½	3-0	0-6	2-0	3-0	2-0	6	1-12	2-12†	0-12	0-12
Moderate cost adequate	7½	1-12	0-2	2-0	4-0	4-8	6	2-8	2-2	1-0	1-0
Liberal	7	1-6	0-2	6-0	4-0	6-0	9	2-8	1-8	1-2	1-2

\*These quantities are translated into household terms under separate headings below.

†Or its equivalent in cheese, evaporated milk, or dried milk.

‡To meet iron allowances, from 30 to 50 per cent of the cereal should be whole grain.

TABLE II. DAILY CONSUMPTION OF MILK

DAILY	NUMBER OF WOMEN	PER CENT
Some, but less than 8 ounces	131	25
8 ounces, but less than 1 pint	198	39
1 pint, but less than 1 quart	172	33
1 quart	13	3

Table II. A very small percentage consumed one quart or more daily. About one-half of this group was made up of women in the highest income brackets. The average was less than one pint daily.

*Potatoes and Sweet Potatoes.*—Potatoes furnish calories at low cost. They are good sources of vitamin B<sub>1</sub>, vitamin C, and iron. Sweet potatoes are particularly valuable for their vitamin A content.

The recommendations in Table I would amount to two servings daily for the low-cost diet, one or two for the moderate-cost diet, and one for the liberal diet. Fifteen women, most of whom were in the low income group, used potatoes at least twice daily (Table III).

TABLE III. POTATOES AND SWEET POTATOES

SERVINGS	NUMBER OF WOMEN	PER CENT
None	14	3
Some, but less than one daily	311	60
One daily, but less than two	174	34
Two or more daily	15	3

*Dried Beans, Peas, and Nuts.*—Legumes, generally, are valuable for protein, iron, and thiamin. They also furnish calories cheaply. They should be used four times weekly in the low-cost diet, three times weekly in the moderate-cost diet, and once weekly in the liberal diet.

Almost one-half the number of women studied used no legumes at all. About two-thirds of those who used them at least four times weekly were in the lowest income group (Table IV).

TABLE IV. DRIED BEANS, PEAS, AND NUTS

SERVINGS	NUMBER OF WOMEN	PER CENT
None	246	48
Some, but less than two weekly	188	37
Two or three weekly	59	11
Four or more weekly	21	4

*Tomatoes, Citrus Fruit or Other Vitamin C Rich Foods.*—Those fruits and vegetables which are good sources of vitamin C can usually be relied upon to furnish other vitamins and minerals as well. Since they may be eaten raw or after short cooking periods, there is not much danger of losing their vitamin content.

TABLE V. TOMATOES, CITRUS FRUIT OR OTHER VITAMIN C RICH FOODS

SERVINGS	NUMBER OF WOMEN	PER CENT
None	12	2
Some, but less than one daily	202	39
One daily, but less than two	214	42
Two or more daily	86	17



The diet of the pregnant woman should contain at least one serving daily of these foods and two if the food budget will permit. Table V shows that a small percentage of the group ate two servings daily. A large number consumed vitamin C foods less frequently than once daily.

*Leafy, Green, and Yellow Vegetables.*—All fruits and vegetables make outstanding contributions to the diet in the way of minerals and vitamins. They help to maintain alkaline reserve, they provide roughage, and they lend color, flavor, and texture to menus. They are not always cheap, and transportation factors affect their cost.

TABLE VI. LEAFY, GREEN, AND YELLOW VEGETABLES

SERVINGS	NUMBER OF WOMEN	PER CENT
None	5	1
Some, but less than one daily	231	45
One, but less than two daily	213	41
Two or more daily	65	13

Leafy, green, and yellow vegetables are important for their iron and vitamin A content. Pregnant women limited to low-cost diets should use them about once a day and those who can afford the moderate cost and liberal diets should have one or two servings daily. Note how few women attained the desire of two servings (Table VI). Almost one-half of these women were in the highest income groups. Those who had none were in the lowest.

*Other Vegetables and Fruits.*—To use the quantities of other fruits and vegetables not mentioned above and suggested in Table I, women in the low-income group should eat them about once daily. Those in the moderate group should have about two servings a day. Those in the liberal group should eat two or three servings daily. Table VII explains how the women in this study met the standards. More than one-half of those eating only one serving daily were in the low income group.

TABLE VII. OTHER VEGETABLES AND FRUITS

SERVINGS	NUMBER OF WOMEN	PER CENT
None	5	1
Some, but less than one daily	139	27
One, but less than two daily	199	39
Two, but less than three daily	113	22
Three or more daily	58	11

*Eggs.*—Eggs contain protein, they are excellent sources of vitamin A and iron, and they provide other minerals and vitamins as well. One egg in some form should be included about once a day in the pregnant woman's diet and more often when food money is not limited. Not many of these women used one egg daily (Table VIII).

TABLE VIII. EGGS

SERVINGS	NUMBER OF WOMEN	PER CENT
None	54	11
Some, but less than one every other day	214	42
3½ per week, but less than 7	177	34
One daily or more	69	13

*Lean Meat, Poultry, and Fish.*—In addition to their protein value, these foods are rich in thiamin, riboflavin, and nicotinic acid. Liver and

lean meat are high in iron content, and liver is an excellent source of vitamin A. All add interest and flavor to the diet.

To meet dietary requirements, pregnant women should have one serving of these foods every other day in the low cost group, one serving daily in the moderate cost group and at least that much and preferably more in the liberal group. Most of these women had at least one serving every day (Table IX).

TABLE IX. LEAN MEAT, POULTRY, AND FISH

SERVINGS	NUMBER OF WOMEN	PER CENT
None	1	(-.2)
Some, but less than 3½ weekly	19	4
3½, but less than 7 weekly	149	29
7, but less than 10½ weekly	243	47
10½, but less than 14 weekly	81	16
14 or more weekly	21	4

*Fours and Cereals.*—No attempt was made in this report to measure the amounts of bread and cereal consumed. The interest was centered instead on the amount of whole grain cereals and bread. These are important for their vitamin B and iron content. Table X shows how infrequently these women ate at least one-half of their bread and cereals in the whole grain form.

TABLE X. WHOLE GRAIN CEREALS AND BREAD

AMOUNT	NUMBER OF WOMEN	PER CENT
None	107	21
Some, but less than ½ of intake	317	62
½ or more of intake	90	17

*Fats.*—Table XI shows how many women used one ounce or more of butter or fortified oleomargarine daily. Butter is important for vitamin A as well as for the calories it yields. Some women, most of whom were private patients, used cod-liver oil routinely during pregnancy.

TABLE XI. BUTTER AND FORTIFIED OLEOMARGARINE

AMOUNT	NUMBER OF WOMEN	PER CENT
None	20	3.9
Some, but less than one ounce daily	383	74.5
One ounce or more daily	111	21.6

*Sugars.*—Molasses, honey, brown sugar, and unrefined syrups are to be desired over refined sugar. Only 63 women (12 per cent) used the unrefined forms of sugar.

A study of the food habits of 514 pregnant women in Philadelphia reveals principally a lack of knowledge of adequate food values. A slight effort on the part of obstetricians in nutrition education for pregnant women would bring about good results not only for the mother and fetus, but for the entire family as well.

## SUMMARY

Only 3 per cent of the women in this group consumed one quart of milk daily. Twenty-five per cent of them had less than 8 ounces daily.

Only 59 per cent of them chose one serving or more of citrus fruits and vitamin C rich foods daily.

Only 54 per cent ate at least one leafy, green, or yellow vegetable daily.

A large number of women did not realize the need in the diet for potatoes, legumes, and other vegetables and fruits not mentioned above.

Only 47 per cent consumed three or four eggs weekly.

Twenty per cent reported an intake of lean meat, poultry, and fish of one and one-half servings daily.

Seventeen per cent ate one-half of their bread and cereals in the whole grain form.

Only about 21 per cent used one ounce of butter or fortified butter substitute daily.

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## POSTMENOPAUSAL ENDOMETRIOSIS

### A CASE REPORT AND REVIEW OF THE LITERATURE

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**I**T IS insufficiently emphasized in the literature on endometriosis that typical lesions are not infrequently found in women past the menopause. The existence of a sizable group of noncyclical women presenting these lesions deserves consideration, because one might not predict such a group from accepted concepts of the pathogenesis of the disease and further, because the origin and fate of such tumors are of concern in prognosis and treatment of these patients.

Pathologic diagnosis of the lesion depends on the demonstration of epithelial elements closely resembling endometrium, in an abnormal location. Many theories have been advanced to account for the presence of this ectopic tissue, and, although each seems to explain certain clinicopathologic observations, the accumulated body of evidence contains data irreconcilable with any single theory. This suggests that no single mechanism is universal in the pathogenesis of this disease. Whether, however, one attributes the genesis of the lesion to (a) diverticular invasion of the uterus by normal endometrium (Cullen), (b) activation of celomic rests (Iwanoff, Novak), (c) epithelial heterotopy dependent

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on inflammatory or hormonal stimulus (Meyer), (d) lymphatic or hematogenous spread (Halban), or (e) retrograde tubal menstruation (Sampson),\* it seems logical to concede that its subsequent growth and invasiveness are dependent on the same hormonal influences on which the growth of normal endometrium is contingent. The lesion, as observed in the cyclical woman, is characterized by symptoms indicating cyclical growth activity, and by the histologic pictures of proliferation and edema, desquamation and hemorrhage, closely paralleling the changes of the normally situated endometrium. Moreover, endometriosis before the menarche is exceedingly rare.

Not only does hormonal stimulation appear to be necessary for the growth of these tumors, but evidence of hyperestrinism is to be found in a large proportion of these patients, as previous authors have argued.<sup>14, 19</sup> In the absence of laboratory data, the evidence on this point rests on the coincidence of endometriosis with endometrial hyperplasia and follicular cysts, lesions which are probably related to hyperestrinism. Uterine fibromyomas, also possibly related to endocrine causes, are, similarly, quite frequently associated.

We have reviewed the records of all cases of uterine endometriosis (adenomyosis) surgically treated in this hospital during the nine-and-one-half-year period from January, 1933, to July, 1941, with special attention to the age, menstrual status, symptomatology, and associated pathology. An analysis of the associated findings in the 203 cases (Table I) reveals a statistically significant incidence of the above-mentioned lesions; much in excess of that to be expected were these lesions and endometriosis etiologically independent. This finding is in qualitative agreement with those of other reviewers (Table II).

The above considerations make it reasonable to conclude that the growth and maintenance of ectopic endometrial foci are dependent on hormonal stimuli. Paradoxically, however, these lesions are found in women past the menopause, a state characterized by hypoplasia and atrophy of the genital epitheliums. In this series of 203 cases of adenomyosis, there are found 23 patients in the menopausal group, employing as criteria either amenorrhea for periods in excess of six months, or definite symptoms and signs of the menopausal state. In previously published series of cases, the presence or absence of the menopause is not indicated, but, by the arbitrary selection of age 50 as the onset of the menopause, one may obtain a crude estimate of the number of menopausal patients in such series, for purposes of comparison. This would seem to be an acceptable procedure, inasmuch as the number of cyclical patients over that age is commonly much fewer than the number of menopausal patients below that age. In Table III it will be noted that 10.6 per cent of the cases fall into the menopausal group, an incidence much higher than one might expect.

\*See reference 10 for a review of these theories.

TABLE I. ASSOCIATED PATHOLOGY IN 203 CASES OF ADENOMYOSIS

LESION	NUMBER OF CASES	PERCENTAGE
No associated lesion	21	
Uterine lesions	158	
Fibromyoma	148	73.0
Myosarcoma	3	1.5
Carcinoma	2	1.0
Hematometra with cervical stricture	1	0.5
Double uterus	1	0.5
Normal pregnancy	1	0.5
Hydatid mole, chorioadenoma destruens	1	0.5
Chorioepithelioma	1	0.5
Endometrial lesions	54	
Hyperplasia	26	13.0
Polyp	28	14.0
Ovarian lesions	74	
Follicular cyst	44	22.0
Chocolate cyst	9	4.5
Simple cyst	9	4.5
Serous cyst	3	1.5
Dermoid cyst	3	1.5
Papillary cyst, serous	2	1.0
Papillary cyst, pseudomucinous	2	1.0
Theca cell tumor	1	0.5
Granulosa cell tumor	1	0.5
Miscellaneous	11	
Endometriosis of tube	5	2.5
Parovarian cyst	3	1.5
Endometriosis of pelvic peritoneum	1	0.5
Endometriosis of abdominal wound	1	0.5
Endometriosis of appendix	1	0.5

TABLE II. ASSOCIATED PATHOLOGY

AUTHOR	NO. CASES OF ENDOMETRI- OSIS IN SERIES	PERCENTAGE CO-INCIDENCE		FIBROIDS
		HYPERPLASTIC ENDOMETRIUM	FOLLICULAR CYSTS	
Waters <sup>18</sup>	18	-	-	33
Witherspoon <sup>20</sup>	44	90	100	-
Henderson <sup>13</sup>	82	24.3	-	-
Jeffcoate <sup>14</sup>	113	71	-	21
Allen <sup>1</sup>	112	70	-	41
King <sup>15</sup>	114	50	-	-
Smith <sup>17</sup>	159	42	-	52
Dreyfuss <sup>4</sup>	162	29	-	-
Bland <sup>2</sup>	172	-	-	54
Fallas and Rosenblum <sup>5</sup>	260	10.7	3	41
Counseller <sup>3</sup>	884	-	-	54
This series	203	13	22	73

TABLE III. AGE DISTRIBUTION

AUTHOR	NO. OF CASES	UNDER 20	20-40	40-50	OVER 50	% OVER 50
Dreyfuss <sup>4</sup>	152	0	43	96	13	8.6
Fallas and Rosenblum <sup>5</sup>	260	0	139	102	20	8.0
Bland <sup>2</sup>	276	1	139	110	26	9.6
Counseller <sup>3</sup>	884	0	333	443	108	12.2
This series	203	0	75	107	21	10.3
Total	1,775					
Average						10.6



We have recently encountered a patient classed in this group, and have been able to study the case clinically and endocrinologically.

#### CASE REPORT

B. V., a 63-year-old white woman, was admitted to Mount Sinai Hospital on Sept. 18, 1941, to the gynecologic service of Dr. S. H. Geist. She complained of aching right lower quadrant pain and backache present during the week prior to admission. Ten months previously she had visited a physician for a similar complaint and was told she had a right ovarian cyst. She remained symptom-free for seven months thereafter, when she had a sudden bout of vaginal bleeding lasting two days. Subsequently she was perfectly well until the present episode.

Menses had been entirely normal, without dysmenorrhea or excessive flow. Flow began at the age of 13, occurred every thirty days and lasted for three days. There were three pregnancies with two full-term deliveries. Last menstrual flow occurred in 1931 at age of 53, and during the following three-year period she had mild menopausal symptoms including hot flushes.

*Physical Examination.*—Patient was a small white female with graying hair, normal in distribution. Heart and lungs were negative. Breasts were atrophic. Thyroid was unenlarged. Pelvic examination: "Normal introitus. Cervix small, lacerated. Behind and somewhat to the right of the uterus is the lower pole of a soft, elastic, semicystic mass. The adnexa are not distinctly palpable."

*Laboratory Examination.*—Sedimentation rate was twenty-eight minutes (normally over 60 minutes). White blood count was 7300, and hemoglobin 71 per cent.

*Operation.*—The right broad ligament was occupied by a plum-sized cyst. This, together with the right tube and ovary, had undergone torsion, and displayed a hemorrhagic, infarcted appearance. The left adnexa were negative, the ovary appearing small, yellowish-white and atrophic. The uterus was slightly enlarged by the presence of a fundal adenomyoma and a small fibromyoma.

*Pathologic Study.*—Examination revealed an infarcted papillary parovarian cyst, with infarcted tube and ovary, on the right side. The left ovary showed atrophy; no active follicles or follicular cysts were present. Fat stain failed to demonstrate lutein tissue. The uterus contained an area of adenomyosis (Fig. 1) and a small fibromyoma. The endometrium consisted of a single layer of cells with no evidence of convolution or glandular activity (Fig. 2). Glycogen stain failed to reveal significant amounts of glycogen.

#### *Endocrinologic Study.*—

*Vaginal smear:* The individual cells were, on the average, smaller than those seen in smears from cyclical women.

*Vaginal biopsy:* There was moderate layering but no cornification. In some areas the thickness approached that seen in cyclical women, but for the most part the appearance was that of involutional hypoplasia.

*Gonadotropic hormone studies:* Urine extraction and bio-assay for gonadotropin<sup>s</sup> revealed a titer of at least 4 rat units per day, which is in the postmenopausal range. The ovarian responses were of the character associated with castrate gonadotropin.

*Estrogenic hormone studies:* Blood extraction and bio-assay<sup>9</sup> failed to demonstrate the presence of estrogens in the amounts found during the latter half of a menstrual cycle, the extract of 30 c.c. of whole blood failing to elicit a threshold response in castrate rats.

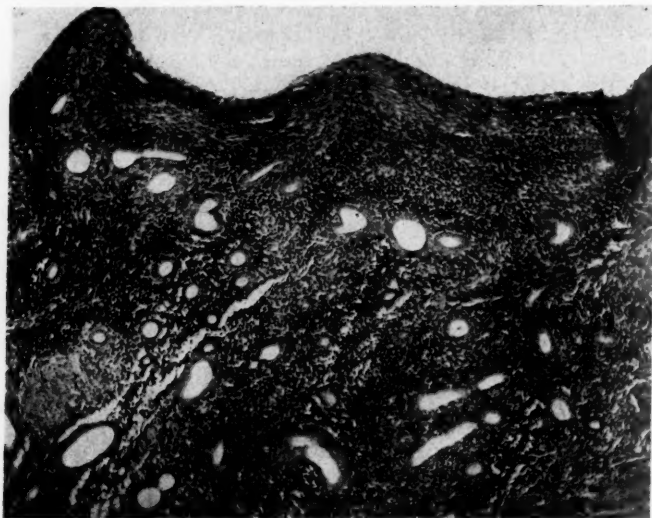


Fig. 1.—Section of the adenomyomatous area ( $\times 90$ ).

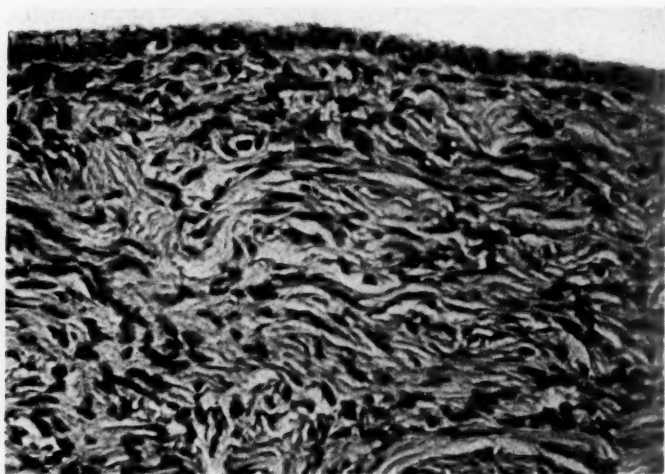


Fig. 2.—Section showing endometrium in a state of postmenopausal atrophy ( $\times 600$ ).

#### DISCUSSION

In the light of our previously outlined views of the pathophysiology of endometriosis, the sizable group of postmenopausal cases demands elucidation. Consistent with these views, the explanation suggests itself that the lesions found represent residua of tumors which had developed during the cyclical period, and thereafter have persisted in

relative quiescence and regression. It may indeed be that extragonadal, possibly adrenal, sources of estrogenic steroids supply a stimulus permitting continued, decelerated growth. The occasional finding of vaginal mucosa without regressive change<sup>11</sup> and the extraction of significant amounts of estrogenic substance from the urine of some women past the menopause<sup>6</sup> or after castration<sup>7</sup> would indicate that the menopausal state is not invariably one of complete estrin deprivation. It may further be reasoned that androgens, which are excreted in increased amounts with the advent of the climacteric,<sup>12</sup> may possess some estrogenic potency in the human being, although very little in the rodent. In this connection the demonstration of the estrogenic activity of desoxycorticosterone<sup>16</sup> is of interest. In general, however, it is true that estrogens are in very low titer in most menopausal women, and play a questionable role in the metabolism of these tumors.

On clinical grounds, the growth activity of the lesions appears to be in abeyance. In none of the 23 cases here cited were there symptoms attributable to the adenomyoma itself; in all cases operation was performed to relieve symptoms due to other pathology (fibroids, prolapsus, etc.). Certainly there is no evidence, either in our studies or in the literature, to indicate that these tumors can originate *de novo* after the climacteric, or even persist in active, symptom-producing growth.

In summation, the present investigation would indicate that, although uterine endometriosis is not infrequently present in the postmenopausal woman, such lesions are to be regarded as in a state of regression and atrophy, incapable of renewed growth activity. The tumors do not produce symptoms, except, conceivably, as a function of position or size attained during the premenopausal period of development.

#### SUMMARY

1. Theories of the origin of endometriosis are reviewed and the pathophysiologic role of estrogen stimulation is discussed.
2. A series of 203 cases of adenomyosis is presented, of which 23 were in women past the climacteric. An additional case is studied and reported.
3. The origin and fate of such tumors in the postmenopausal woman are discussed.

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### SEXUAL LIBIDO IN THE FEMALE\*

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"The sour, shallow, sexless shrew is an imposter as a wife and her marriage is a fraud."—Jordan.

MANY of the neuroses and ills of womenfolk may be traced to unhappy or unsatisfactory sexual relations. The wife without sexual desire, unless she has histrionic ability or other charms, frequently finds her marital relations strained. So frequently the complaint of frigidity is dismissed by the physician as unworthy of consideration or as a condition about which nothing can be done. Frigidity may be absolute; it may be relative. When frigidity is relative, desire is present but coitus does not culminate in complete gratification. Frigidity may be due to psychogenic or anatomic factors with resultant dyspareunia or vaginismus. The need for a better understanding of this problem cannot be questioned. The medical complexities and the social implications are many. The successful treatment of frigidity may circumvent the disintegration of a marital union or prevent a man's search of extra-marital adventure with its dangerous consequences. The literature is almost void of contributions to the subject.

Libido is a highly complex function in which psychologic, anatomic, neurologic, sentimental and hormonal components play important roles. The role of the hormonal component has not received due attention. The experiences gained by our group in evaluating the effects of pellets of testosterone propionate implanted in over 55 women and pellets of pure crystalline progesterone implanted in 16 women lead us to believe that love, libido, and marital harmony are frequently closely associated. At

\*Read by the senior author at a meeting of the Talladega County Medical Society, Talladega, Alabama, December 16, 1941.

times, it appears, libido is merely a phenomenon depending on well-defined chemical substances.

In certain animals, the female of the species will receive the male in coitus only when in heat or estrus, and this is timed with follicle maturation. The period of heat in the dog lasts for a little longer than one week and occurs at six-month intervals. The cycle of the female chimpanzee simulates that of the human female. Unlike the latter, however, the chimpanzee will accept the male only during the height of genital turgescence, which corresponds to the phase of follicle maturity. During the luteal phase regressive changes set in, at which time she will fight off the male. It may be said then, as far as libido is concerned, that the corpus luteum hormone is opposite in its action to estrogens. This fact receives further corroboration in the work of Gillman<sup>1</sup> who has shown that the perineum of the baboon is a sensitive indicator in experiments involving the use of female sex hormones. Deturgescence in the normal adult female baboon is a positive phenomenon, due to the presence of progesterone and not to the absence of estrogens. Progesterone administered in total doses of 10 mg. or less will cause depression of the turgescence of the perineum.

The human female is unlike the dog or the chimpanzee. In fact, certain females exhibit marked nymphomaniacal tendencies during the week before the onset of menses. These same individuals frequently exhibit marked evidence of premenstrual tension.<sup>2</sup> Endometrial biopsies often reveal imperfect progestinal types of endometria and blood estrogen titers may be somewhat higher than normal. It may be that in these cases excessive estrogen overrides corpus luteum activity. A high kidney threshold for estrogen excretion may be the prime fault. Following the administration of parenteral progestins to these patients in doses of 1 to 5 mg. every three to seven days or oral progesterone in 5 mg. doses during the last half of the menstrual cycle, there is frequently noted a detumescence of the sexual urge.<sup>3</sup>

Although estrogens have been administered with resultant increase in libido, nevertheless many women without sexual desire do not seem to respond to massive doses. Frequently, when estrogens fail, positive results have been obtained with testosterone propionate. Seventy-five to 200 mg. injected parenterally has frequently proved aphrodisiacal. This point is at variance with other investigators.

Rubenstein and his associates<sup>4</sup> have recommended testosterone propionate for the treatment of morbid sex cravings. They used 25 mg. at varying intervals for the relief of exaggerated sex urge. All the patients in their series had marked premenstrual tension. Abarbanel<sup>5</sup> also believes that nymphomania may be relieved with testosterone propionate. Some hold the opinion that androgens neutralize the action of estrogens, hence its value in the therapy of nymphomania. Testosterone propionate does not depress libido in the female. Wilson<sup>6</sup> in treating a young woman used a total dosage of 4,800 mg. of testosterone propionate over



thirteen months. In spite of the virilization of the patient, there was no loss of libido. In July, 1940, one of us<sup>7</sup> (R. B. G.) reported that the administration of 10 to 50 mg. of testosterone propionate in divided doses during the latter half of the cycle was sufficient to bring about an abatement of premenstrual tension. This adjustment probably relieves the nymphomaniacal tendencies of some women at this time.

Silberman and his colleagues<sup>8</sup> observed no effects upon libido in a group of menopausal patients treated by testosterone propionate. Salmon<sup>9</sup> noted that many of his patients experienced definite increase in libido during the course of injections and for several weeks thereafter. In many of these patients he found the clitoris erythematous and very sensitive to touch. The majority of these cases received more than 500 mg. of pure crystalline androgenic substance in one month. Recently, we have been able to confirm the impression of J. R. Groome<sup>10</sup> that frigidity may be due to a local defect of the clitoris which may be benefited by local application of testosterone propionate ointment. In a previous communication we reported that the subfascial implantation of testosterone propionate pellets in dosages varying from 25 to 145 mg. in a group of 10 patients was attended by a definite increase in sexual libido in every patient of the series.<sup>11</sup>

The increase in libido in the female following the administration of chemically pure androgenic substance in one form or another must be the result of a specific pharmacologic effect. The action may be mediated through minor changes in electrolyte balance or the effect may be directly on specific organs. Hartman<sup>12</sup> noted that testosterone invariably had an estrogenic action on the sex skin of the female monkey. The sex skin was always brilliant red. In this respect he found progesterone antagonistic to estrin. Testosterone did not antagonize the action of estrogens. Even in pregnancy, Hartman was able to blanch the sex skin with a sufficiently high dosage of progesterone. However, the concurrently injected estrogens and testosterone or both were sufficient to override the blanching action of the progesterone. In a series of 16 patients, progesterone pellets were implanted for various gynecic disorders. We were impressed with the fact that there was a decided depression in the sexual libido of several in whom it had been markedly exaggerated. One such case is described:

W. F., 23 years of age, unmarried, was referred to the endocrine clinic from the psychiatric clinic of the University Hospital. Her complaints were dysmenorrhea, nervousness, fainting spells, morbid restlessness and exaggerated sexual impulses. A pellet of 150 mg. of progesterone was implanted subfascially. Soon after there followed a decrease in her nervous tension state, a reduction in fainting spells from two to three per week to one in four or five weeks, amelioration of the dysmenorrhea and above all so marked a reduction in sexual desire that she no longer had any desire to "run around." She became fonder of her home and wished to do her share of the family chores. With the diminution in her libido, the haze seemed to clear; she saw the evil of her ways and was now repentant.

EVALUATION OF EFFECTS OF ANDROGEN PELLETS IMPLANTED IN  
55 WOMEN

One to four pellets of testosterone propionate weighing 25 to 200 mg. each were implanted subfascially in dosages from 25 to 400 mg. Statistics are available on 55 women between 22 and 53 years of age from whom information was obtainable as to their sexual urges before and after implantation. The patients have been followed from four to twenty-four months. Arrhenomimetic phenomena did not develop in any of these patients. Loeser obtained marked increase of libido in the patients in whom he implanted pellets of testosterone propionate, but his dosage was excessive, 600 to 1,500 mg., and he obtained signs of masculinization. We found that a 100 mg. pellet was the ideal dosage.

It seems impossible to increase libido in some psychologically frigid women who never have experienced sexual desire. On the other hand, restoration of the libido easily occurred following implantation in those women who at some time have known libido. Many married women volunteered the information that their loss of sexual desire led to marital discord. Following pellet implantation there was a return of coital pleasure which often terminated in orgasm. A re-awakened interest on the part of the husband usually followed, and husband and wife once more fell in love. The following phrase, trite and common, found frequent expression, "My husband treats me kindlier, is more attentive now and stays home evenings." In those women who had a marked to moderate degree of sexual desire before implantation all noted either no significant change or further increase in sexual pleasures. In two women with normal libido, there was a temporary decrease in sexual desire for several weeks immediately after pellet implantation, then there was a resurgence of the libido to a greater degree than that before the implantation. In several it was noted that the libido returned to the pre-implantation status by the end of the third to eighth month. In the majority, however, it persisted long after the pellets had been absorbed. Table I indicates that following implantation of testosterone propionate pellets there was an increase in sexual libido in most cases, while a resurgence of libido could be expected in almost every one of those who once had libido but had lost it.

TABLE I

	NO.	DEGREE OF LIBIDO BEFORE PELLETS	AFTER PELLET				
			MODERATE INCREASE	MARKED INCREASE	TEMPORARY INCREASE	NO CHANGE	DECREASE
Group 1	7	Very little or never had libido	1	4	1	3	
Group 2	23	Once had libido but lost it	8	13	1		
Group 3	14	Mild to moderate libido	2	6		6	
Group 4	10	Good to excessive libido			1	8	1*

\*Nymphomaniacal reduced to normal.

## CASE REPORTS

The following brief case reports are selected to illustrate the points in question:

CASE 1.—C. F., aged 41 years, had menorrhagia and massive fibromyoma. Once had normal libido but had lost it. A pellet of 25 mg. of testosterone propionate was implanted twenty months ago. Her libido improved remarkably and has remained good to the present time.

CASE 2.—W. F., aged 30 years, married six years, complained of dysmenorrhea and dyspareunia. She never had any libido. In the four months since implantation of two 200 mg. pellets of testosterone propionate she has experienced marked increase in sexual satisfaction and feels much more in love with her husband.

CASE 3.—C. F., aged 25 years, with menorrhagia and fibromyoma, had three pellets, totaling 145 mg. of testosterone propionate, implanted subfascially. Before this procedure her libido was mild and she had sexual intercourse with her husband once or twice per week. Two months after implantation she volunteered the information that she had sexual relations once or twice per night. Her libido has remained very good throughout the fifteen months of her observation period.

CASE 4.—W. F., 40 years of age, complained of menorrhagia. Three pellets of testosterone propionate, totaling 146 mg., were implanted one year ago. Before implantation her libido was good. After this procedure it became excessive, but at the end of six months the libido returned to its pre-implantation status.

CASE 5.—W. F., 42 years of age, married 26 years, para ii, gravida iii. Her menstrual history was inconsequential except that she had had almost continuous flooding for three months. She also had urinary frequency, dysuria, hot flushes, and had lost 25 pounds in weight with her bleeding spell. Routine medication failed to arrest the menorrhagia. Two pellets, totaling 205.2 mg. of testosterone propionate, were implanted subfascially. Suction curettage before implantation revealed a hyperestrogenic endometrium. Study of the vaginal secretions revealed the presence of trichomonads. Libido before implantation was poor. Bleeding stopped five days after implantation. Two weeks later an improvement in her libido was noted. One month after implantation the patient found that her libido was much better and her sense of well being had improved. Her menstrual periods became regulated, and the disturbances of micturition were alleviated. At the end of six months, when asked about her sexual nature, she answered "it was better than it had ever been in her life and that she and her husband were more in love with each other." Her weight increased 12 pounds, she was sleeping better, and had no hot flushes. Several weeks later she noted a sudden diminution in her libido. She regretted this very much for her home life and relations with her husband had improved so much. She hesitated to relate these facts for she said "It was not good talk for a church woman." Fortunately this was only a temporary depression of libido for it soon returned and eight months after pellet implantation still remains at a good level.

## CONCLUSIONS

It must be admitted that sentimental, psychologic, and anatomical factors greatly influence the libido, nevertheless the role of the hormones is such that libido may be spoken of as a test tube chemical equation. Progesterone, the hormone of the corpus luteum in chemically pure crystalline state may be administered to depress excessive libido when present; on the other hand, chemically pure androgenic substances when properly administered decidedly increase the well being of the patients as well as the libido. Although the parenteral and oral administration of compounds of testosterone was frequently followed by increase in sexual urge, it was found that more consistent results could be obtained by pellet implantation. One hundred milligram dosage proved ideal. Pellets of testosterone propionate implanted subfascially are capable of providing a continuous prolonged nearly natural physiologic action. No fear of virilization need be entertained with this method and in dosages up to 400 mg. In almost every patient who once had known libido, a resurgence followed testosterone propionate pellet implantation.

These facts may provide a working basis for treatment. The psychotic tendencies of the nymphomaniac, the neuroses and unhappiness of the frigid female, and the problems of the incompatible couple, with their sociologic implications, are amenable to hormone therapy. There is much that can be done for the individual whose life may be colored by sexual frustration or sexual excess. The potentialities for correcting such maladjustments and for bettering human relationships may lie in the physician's hands.

The pellets of testosterone propionate are a product of Ciba Pharmaceutical Products, Inc. The pellets of pure crystalline progesterone are a product of Schering Corporation.

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## SCOPOLAMINE IN OBSTETRICS

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MUCH has been written concerning analgesia in labor and many diversified opinions regarding its merits have arisen. In view of these controversies, a report based upon the study of a single drug, namely, scopolamine, should be of value in considering the comparative effectiveness of the barbiturates and hypnotics in obstetrics.

Objections to the use of scopolamine have been made on the grounds that it is dangerous, because it lengthens the labor period and increases susceptibility to post-partum hemorrhage, that its action is uncertain, that there is great individual variation (the same dosage affecting patients differently), that it is responsible for a high percentage of operative deliveries, that it causes fetal asphyxia or cerebral damage, and that it is not applicable in private practice.

The successful results on 2,200 cases, reported by Dr. Bertha van Hoosen in 1928, did much to popularize this method of analgesia in labor. A similar technique has been employed in our cases, and the gratifying results obtained indicate the efficacy and safety with which this drug may be used in obstetric practice.

### TECHNIQUE OF ADMINISTRATION

The data presented here summarize the effects upon 1,481 private patients, 739 primiparas and 742 multiparas, personally attended by me at the Woman's Hospital of Detroit from 1930 to 1941.

1. *The Skin Test for Sensitivity.*—This is usually done sometimes during the last month of pregnancy. Scopolamine ( $\frac{1}{4,000}$  gr.) is injected intradermally on the forearm. The reaction is observed within twenty minutes and is graded on the basis of the degree of redness surrounding the site of injection. If the diameter of the red area is 1 cm., the reaction is labeled 1-plus, etc. A definite correlation between the reaction and sensitivity to the drug exists. The degree of excitement during labor under scopolamine is usually proportional to the amount of skin reaction. It is certain that a patient who exhibits a 4-plus reaction will prove to be hyperexcitable during labor. However, such a reaction need not be regarded as a contraindication to the use of the drug, but rather as a warning that the patient may require a greater amount of attention during labor than would otherwise be necessary.

2. *Time of Administration.*—The drug is injected subcutaneously to permit of slow action, when the pains are recurring at regular intervals (every ten minutes), when uterine contractions are strong, of



good character and frequency (lasting forty-five seconds), and when the cervix is effaced and dilatation has begun.

3. *Dosage.*—Because scopolamine is eliminated from the body in two hours and because of some occasional individual variation in the effectiveness of the drug, a moderate dosage has been standardized by van Hoosen. This dosage may be used judiciously in all normal deliveries. Three  $\frac{1}{100}$  gr. doses are administered within one hour (e.g., 1, 1:30, and 2:00), and the drug is effective to the point that the patient becomes unconscious of her surroundings. To maintain narcosis indefinitely, the same amount ( $\frac{1}{100}$  gr.) is repeated every two hours, counting from the time the third dose was injected. Repeated injections at two-hour intervals eliminate the necessity of various criteria for guidance in regulating the dosage, such as, pupillary dilation, memory tests, ataxia, or the reappearance of pain. Before each injection, however, a check should be made on the pulse and temperature of the mother, and the heart tones of the fetus.

Variations and individual differences establish a personal equation in the number of doses required. In our series of 1,481 cases, the injections ranged from 1 to 26, the latter without harmful effects or damage of any kind.

#### DOSES OF SCOPOLAMINE

TABLE I. NUMBER OF DOSES OF SCOPOLAMINE

DOSES	3 OR LESS	4-6	7-9	10-12	13-15	16-18	19-21	22	26
Primipara	192	295	97	44	12	4	1	2	1
Multipara	394	195	42	7	2	2	1		

The average dosage was five. In the primiparas, the smallest number of doses was 3, the largest 26. In the multiparas, the smallest number was 1, the largest 21, and the average was 3.

In most cases reported here, ether was administered as a routine, although I personally consider the gases to be more satisfactory. With gas, the oxygen can be controlled better in the mixture. Such anesthetics as ethylene,  $\text{NO}_2$ , cyclopropane, in the order named, given with helium mixture, by skilled anesthetists, will improve the condition of babies at birth. In using ether, the mask should be removed from the patient's face just as soon as the child's brow appears over the perineum.

#### REACTION TO THE DRUG

The action of scopolamine does not become manifest until about one-half hour after the second injection. Therefore, no reaction is usually observed until after the administration of the third dose. Maximum narcosis is produced in one and one-half hours, the effects being:

1. *Sedation.*—The patient is generally tranquil. The head feels heavy, the face is flushed, the pulse and fetal tones are more rapid, and breathing is regular.

2. *Pulse.*—The pulse rate showed a slight increase one hour after the first injection. This is to be expected because of the possible vasomotor stimulation. This increase is followed by a decrease one hour before delivery, and a leveling off or an approach to normalcy one hour after delivery. No serious variation in the pulse rate is seen.

3. *Respiration*.—Clinical doses of scopolamine stimulates respiration slightly, producing a more shallow, regular breathing. No appreciable change was observed in either direction.

4. *Blood Pressure*.—Examination after delivery showed no variation from the rate of pressure taken upon admission to the hospital. Only a few cases showed a slight tendency toward an increase in pressure.

5. *Temperature*.—A tendency for the temperature to show a slight increase was observed.

6. *Diminished Salivary Secretions*.—Thirst, dryness of the mouth and throat, and occasional enlargement of the uvula have been observed. The uvula may swell to five or six times its normal size, and may appear markedly reddened. The redness may persist for several days. Argyrol swabs or throat irrigations will correct this condition.

7. *Visual Disturbances*.—Blurred vision or faulty accommodation commonly occurs, but usually disappears from twelve to twenty-four hours later.

8. *Vomiting*.—This is not an especial characteristic of scopolamine anesthesia. Patients in labor may vomit without anesthesia of any kind.

9. *Retention of Urine*.—This condition occurs, but not specifically as a result of this drug.

10. *Excitement*.—Generally, excitement is reduced and the patient is tranquil and drowsy. However, on rare occasions, the patient may become extremely excitable, as we have previously mentioned, so as to require the vigilance of competent attendants. Of 1,301 recorded cases, there were 13 (1 per cent) of extreme excitement during and after medication, 4 of moderate excitement, and 7 of slight excitement. The number of excitable patients is not sufficient to present a very grave problem.

11. *Amnesia*.—Complete amnesia was obtained in nearly every case. (In a few instances, the memory of pain was very hazy or practically negligible.) The scopolamine narcosis was in each case adequate to cover the delivery period. The patients were unconscious of their surroundings, but the voluntary muscles necessary in the delivery were not inhibited in any way by the anesthetic.

#### CARE OF THE PARTURIENT<sup>®</sup>

It is not necessary for the physician to be present at the bedside throughout the entire period of labor, provided he has an able staff of co-workers who keep him constantly informed regarding the progress of the labor. The attendants, however, must be alert. They must adhere strictly to directions as to amount and time of administration of the anesthetic. In warm weather, the patient's pulse and temperature must be taken every two hours, and the fetal heart sounds must be recorded before each dose. Bladder distention and inability to void must be watched, and catheterization performed when necessary. And finally, constant and careful watching is required to prevent the restlessness of an excited patient. Extremely excitable patients require special attention. Among the few instances of extreme excitement previously mentioned, there was one case of injury, the fracture of a metatarsal. Placing the patient in a crib with padded sides and giving a small amount of drop ether help to attain a more tranquil state in the very excited patient.

## RESULTS BASED UPON STATISTICS

TABLE II. NUMBER OF HOURS OF LABOR

Hours	1-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	46-50	61	72	90
Primipara	56	179	178	95	61	27	11	9	6	2		1	1
Multipara	80	244	115	42	22	4	6	6			1		

1. *Length of Labor.*—Of 1,301 recorded cases, in which the length of labor was carefully timed, 655 were primiparous and 646 multiparous. The shortest primiparous labor was two hours, the longest ninety hours, and the median, twelve hours. The shortest multiparous labor was two hours, the longest, sixty-one hours, and the median six and one-half hours.

2. *Loss of Blood.*—Uterine bleeding was never excessive with scopolamine anesthesia, except in rare cases where gynoplastic repair of old lacerations followed. In fact, the tendency to hemorrhage is less than with any other drug which we have used.

3. *Post-partum Course.*—Scopolamine has no ill effect whatever upon the puerperium. With the possible exception of an occasional complication arising from subsequent surgical involvement, the convalescence period of these patients was smooth and rapid. Of 1,300 recorded cases, there were only 9 post-partum hemorrhages (0.7 per cent). Because of the absence of shock or exhaustion, the patients seem to make quicker recovery than those who have been delivered without this drug. Despite the drying effect and limitation on the mucous secretions during labor under scopolamine influence, lactation does not seem to be affected.

TABLE III. VARIOUS TYPES OF DELIVERY

	RECORDED CASES	NOR- MAL	LOW FOR- CEPS	MID- FOR- CEPS	HIGH FOR- CEPS	BREECH EX- TRACT	PODALIC VERSION	CESA- REAN SECTION	MOR- TALITY
Primiparas	654	284	266	17	1	26	45	13	2
Multiparas	639	451	88	9	0	19	55	5	
Total per cent		56.76	27.38	2.01	0.07	3.47	7.73	1.46	0.15

4. *Types of Delivery.*—No tendency toward any one type of delivery as a result of scopolamine anesthesia was observed. Low forceps were often used routinely.

TABLE IV. TYPE OF SURGERY

	RECORDED CASES	EPISIOTOMY (ROUTINE)	PERINEOR- RHAPHY	AMPUTATION OF CERVIX (LOW)	NO SURGERY
Number	1,300	1,059	80	3	137
Per cent		81.39	6.14	0.23	10.53

5. *Surgery.*—In making comparisons with other anesthetics, statistics show that scopolamine does not increase the incidence of operative intervention.

6. *Complications.*—No complications were ascribable to scopolamine narcosis. Among 739 primiparas, complications occurred in only 1.9 per cent; while in 742 multiparas, there were only 1.7 per cent. These

consisted of 2 toxemias, 2 prolapsed cords, 2 suppurative endometritis, 2 pyelocystitis, 1 pyelitis, 1 bronchopneumonia, 3 first-degree lacerations, 1 second-degree laceration, and 9 post-partum hemorrhages.

#### EFFECT UPON THE BABY

That the infant must pay the price for the mother's comfort and that the condition in which the infant is found at birth depends upon the type and amount of anesthesia absorbed by the mother is a fallacy which may have originated in the fact that the danger to the child, heretofore, was due to the simultaneous use of several drugs in obstetric analgesia. An anesthetic effect upon the infant may thus be produced. The drugs used may not have been antagonistic in their action on the respiratory center, but rather cumulative in effect. Thus, the result was usually one of fetal toxicity and fetal asphyxia. With the use of scopolamine alone, we have seen no ill effects upon the newborn infant.

TABLE V. INFANT BREATHING

	CASES	SPONTANEOUS BREATHING	NO SPON- TANEOUS BREATHING	REQUIRED RESUSCITA- TION	STILL- BIRTHS	DIED
Number	1,276	1,104	96	75	8	2
Per cent		86.52	7.52	5.87	0.62	0.15

*Condition at Birth.*—a. *Appearance:* The baby is usually pink following delivery under scopolamine anesthesia. The congestion of the surface vessels diminishes the blood supply in the deeper brain structure and this markedly reduces the possibility of rupture of the vessels in the region of the brain. It appears that cerebral injuries are less likely to occur.

b. *Fetal Heart Sounds:* When the fetal heart sounds were heard, the babies, in all cases, were born alive, usually breathing spontaneously.

c. *Oligopnea:* This somnolence is a brief delay in breathing which is occasionally encountered. It is transient and need cause no alarm. The child will promptly and readily respond to stimulation, and keeping it warm is essential for prompt recovery.

d. *Cyanosis:* If supplemental anesthesia is carefully administered, and the baby is well oxygenated as it is delivered, there will be no cyanosis.

e. *Fetal Toxicity:* We have not observed any case of fetal toxicity in this series.

f. *Fetal Asphyxia:* Scopolamine properly administered does not cause this condition, but faulty or improper technique might do so.

g. *Stillbirths:* Of 8 stillbirths, 4 were doubtful with regard to fetal heart sounds prior to injection, and there is no reason to ascribe the others to the anesthetic used.

h. *Resuscitation:* Before we used scopolamine alone, we had used the combination of scopolamine and morphine, supplemented by ether. In one month, it was observed that of 40 babies delivered, 15 required resuscitation. With scopolamine alone, a comparison with 40 babies was made the following month, at which time only 4 required resuscitation. The agents most frequently used for this purpose were: tracheal catheter, coramine, alphalobeline, metrazol injection, caffeine or adrenalin, and oxygen from a tank tube and funnel.

i. *Fetal Mortality*: Our fetal mortality is extremely low, being 0.13 per cent. With controlled scopolamine narcosis, fetal deaths are definitely diminished and the few deaths which did occur had other very specific causes.

j. *Mental Development of the Child*: Cerebral injuries at birth cannot be attributed to scopolamine analgesia. Where injuries occur, a review of the case would undoubtedly reveal etiologic factors, such as rapid, violent labor, difficult forceps delivery, etc. The drug itself has no effect whatsoever upon the mentality or development of the infant. The children whom we have delivered under scopolamine several years ago, and whom we have followed up, are as well developed physically and alert mentally as any other group of normal children. These children have now reached the school age and although the psychometric studies which we are now making of the children have not as yet been completed, the results so far obtained reveal a very superior rating, due, of course, to their respective innate capacities. We can only report what we have observed, namely, that no mental impairment resulted from the use of scopolamine.

#### CONTRAINDICATIONS

1. *Physical Condition of the Patient*.—Certain conditions have been listed in which scopolamine is considered contraindicated, some of which, in our experience, we have not found justifiable. We feel that in such cases as weak fetal heart sounds, expected short labor, disproportion between the fetal head and the mother's pelvis, premature cases, or controlled Graves' disease, scopolamine produces no ill effects. Even in tuberculosis, if the patient has undergone a phrenic operation, or thoracoplasty, as long as there is no intense activity of the lesion, scopolamine may be used with comparative safety.

There are, however, some instances where the use of scopolamine is unwise for very obvious reasons: In acute respiratory disease, where the inhibitory action upon mucous secretions would produce a drying effect; in certain cardiac or circulatory diseases, such as coronary or acute decompensation (although cases of compensated mitral lesions seem to tolerate the drug rather well); in active eclamptic convulsions, it is better to keep the blood pressure depressed and avoid any possibility of excitement which the drug may produce; in active toxic goiter, the already too rapid pulse might be stimulated further; in acute or subacute nephritis, where the drug might have a cumulative effect, its elimination being threatened by impaired kidney function; in pulmonary edema, where no masking of symptoms of a disease so serious in nature, should occur; and in marked albuminuria, where the diminution of secretions by scopolamine would place an added burden upon the kidneys.

2. *Atmospheric Conditions*.—Extremely hot weather is not conducive to favorable scopolamine narcosis. Because of the tendency to raise the patient's temperature, the dosage should be reduced considerably, or omitted entirely. If this type of narcosis is desired when atmospheric temperature is above 90° F., the patient's temperature should be taken hourly. The only maternal deaths occurring in this entire series were during extremely hot weather.

One patient, Mrs. R., primipara, with just minor pelvis, entered the hospital in labor on July 10, 1936, the temperature in Detroit being 102° F. and barometric pressure 29.93. Ninety-one deaths from heat



prostration were reported on that day in the city. The patient's temperature was 99° F. She was given  $\frac{1}{100}$  gr. of scopolamine twice. Before the third dose, her face became flushed, green amniotic fluid escaped from the vagina, dilatation was 2 cm., and the fetal heart tones were irregular (180) and distant. Immediate low section was done under nitrous oxide ether anesthesia. The baby was resuscitated with tracheal catheter, its temperature being 102° F. The mother's temperature continued to rise every hour for five hours. At that time, the axillary temperature was 107° F., pulse 160, and respiration 42. An hour later a twitching of the facial muscles was seen. Consultation confirmed the diagnosis of heat stroke, and twenty-six hours after the section the patient died.

Several other patients admitted to the hospital within the next two days of the heat wave showed an elevation of temperature up to 105° F.

The only other maternal death in our records occurred on Aug. 25, 1932, when the temperature was 91° F., the barometric pressure 30.32. This patient, a 33-year-old primipara, had a spontaneous face delivery of a 6-pound 2-ounce baby after a twelve-hour labor, under 8 doses of scopolamine. Her temperature on admission was 98.2° F., and no temperatures were taken during labor. The baby's temperature at birth was 100° F. The patient went into collapse one-half hour after delivery and died three hours later. While death in this case may have had some relation to the high temperature, it may also have been due to cardiac dilation.

#### COMPARISON WITH OTHER ANALGESICS

Obstetric anesthesia has undergone considerable metamorphosis. Twenty years or so ago, the common practice of administering nitrous oxide at the patient's bedside at each labor pain proved costly for the patient, worked hardships on the department of anesthesia, and the results obtained were only mediocre. With the introduction of intravenous anesthesia, the problem of short labor could be handled with greater facility but, when labor was prolonged over two or three hours, the results were unsatisfactory.

Gwathmey's anesthesia was a great advance, but it also had its disadvantages. The maximum effect lasted three or four hours. Then, it had to be repeated. One could never be certain as to the dosage the patient was getting or retaining. However, favorable results could be obtained in home labors, and therein does its merit lie, for it is still a good method for home deliveries. Evipal by rectum, suggested by Gwathmey, is subject to the same criticism as the original Gwathmey formula.

My personal experience with the various anesthetics has led me to believe that combinations, such as morphine-pantopon, or dilaudid-scopolamine, produce sleepy babies which usually require resuscitation; while nembutal-scopolamine, or any of the barbiturates, seems to produce a greater restlessness on the part of the mother, and the babies are often cyanotic.

Paraldehyde seems to prolong multiparous labors, during which time it is possible for the patient to become restless, sustain serious injury, and require forceps delivery to complete the labor.

Pentobarbital causes undue restlessness and requires very close watching of the patient.

Spinal anesthesia, generally considered dangerous in obstetric practice, has been used occasionally in tuberculous cases by us and we can report very satisfactory results.

We have attempted the use of a combination of a local anesthetic with scopolamine until the baby is delivered, but have found difficulty in maintaining sterile drapes and keeping the patient quiet. It is almost impossible to put the patient in stirrups and to do an episiotomy without having her move her hips during the application of the forceps or the delivery of the child.

Recent scientific work on fetal respiration by Rosenfeld, Snyder and Dreisbach has shown scopolamine to be the only drug in the analgesic narcotic group used in obstetrics that does not depress intrauterine fetal respiration.

Cook County Hospital studies on obstetric anesthesia suggest an increased prothrombin time in babies when barbiturates are used.

#### SUMMARY AND CONCLUSIONS

1. There is no uncertainty regarding the action of scopolamine. Individual variations may be anticipated by the sensitivity test. This drug is rapid in action, constant when standardized dosage is used, and easy to administer.

2. With proper precautions, it is safe for both mother and child. Pulse, respiration, blood pressure, and temperature suffer no ill effects from the drug's action.

3. Amnesia is quite complete. The patient passes the ordeal of labor with a minimum of discomfort and wakes up after delivery well rested.

4. We have seen no alteration or interference with uterine contractions nor with the normal processes of labor under the drug's influence. The mother is not asked to cooperate with the physician or attendants. The contractions continue as they would normally in labor and the patient uses the expulsive forces automatically when the head is on the perineum.

5. The length of labor is not increased. Our data, on the contrary, shows a considerable decrease in this period under scopolamine narcosis.

6. The loss of blood is minimal and the drug is responsible for a lesser tendency to hemorrhage.

7. Convalescence after scopolamine anesthesia is rapid and smooth. The post-partum course is in no way hampered nor affected by its use.

8. Lactation follows in a normal manner. No influence seems to be exerted by the drug.

9. No complications were attributed to this drug. The two deaths which have been described were due to excessive heat and cardiac dilatation.

10. Operative intervention is comparable to any normal curve of distribution in hospital practice.

11. We have seen no evidence of maternal or fetal toxicity or intolerance to the drug.

12. Scopolamine is not harmful to the newborn infant. Cyanosis, fetal asphyxia, or fetal mortality could not be ascribed to this drug.

We feel, therefore, that on the basis of the evidence presented, scopolamine used alone, judiciously, under standardized conditions, by experienced and competent attendants, is the best anesthetic, during labor, which the obstetrician can offer at the present time in hospital practice.

Thanks are extended to Stanley Axelrod, M. L. Axelrod, Lloyd Mallin, and Helen Esser Fenton for their aid in the compilation of the data.

1104 MACCABEE BUILDING

### THE ELECTROENCEPHALOGRAM IN PREGNANCY\*

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THIS study was planned as a preliminary survey of the electroencephalogram in pregnancy with the special purpose of determining whether the electrical activity of the cortex is modified in normal pregnancy and whether there is a difference between the electrical activity of the cortex in normal pregnancy and in pregnancy complicated by toxemia.

#### MATERIAL AND METHOD

The electroencephalograms of 28 pregnant women were obtained. Of these, 20 had normal pregnancies; 3 had mild pre-eclampsia; 4 had severe pre-eclampsia; 1 had eclampsia, and in 1 case the pregnancy was interrupted because of heart failure due to severe rheumatic heart disease. In 17 cases, an electroencephalogram was obtained after termination of pregnancy. Most of the records were taken in the last two weeks of pregnancy and in the first two weeks post partum.

The activity of both frontal, parietal, and occipital areas were recorded on paper with a Grass three-channel electroencephalograph. Unipolar leads were used with the indifferent electrode on the two ear lobes. At the same time, the activity of various cortical areas was recorded as a shadowgram on film, and analyzed into spectra with the Grass frequency analyzer.

#### RESULTS

In all but 3 of the 16 cases where pre- and post-partum records were obtained, cortical activity was slower during than after pregnancy (Fig. 1). In 2 cases, it was unchanged, and in one, it was faster dur-

\*This study was aided by grants from the John and Mary R. Markle Foundation and the Rockefeller Foundation.

ing pregnancy. In 4 cases, a second post-partum record was obtained, two or more months after delivery; in all 4 cases, this record also was faster than the prepartum record. This suggests that the change occurring with pregnancy can be properly regarded as a slowing of cortical activity during and as a return to the patient's usual cortical frequency after delivery. Table II contains further evidence that the deviation is in the direction of slowing during pregnancy. From this table it may be seen that 40 per cent of the patients with normal pregnancy had electroencephalograms which were classified as slow, a much higher incidence of slow records than has been observed in any normal control series. The complete absence of high-voltage fast records in this group is also noteworthy.

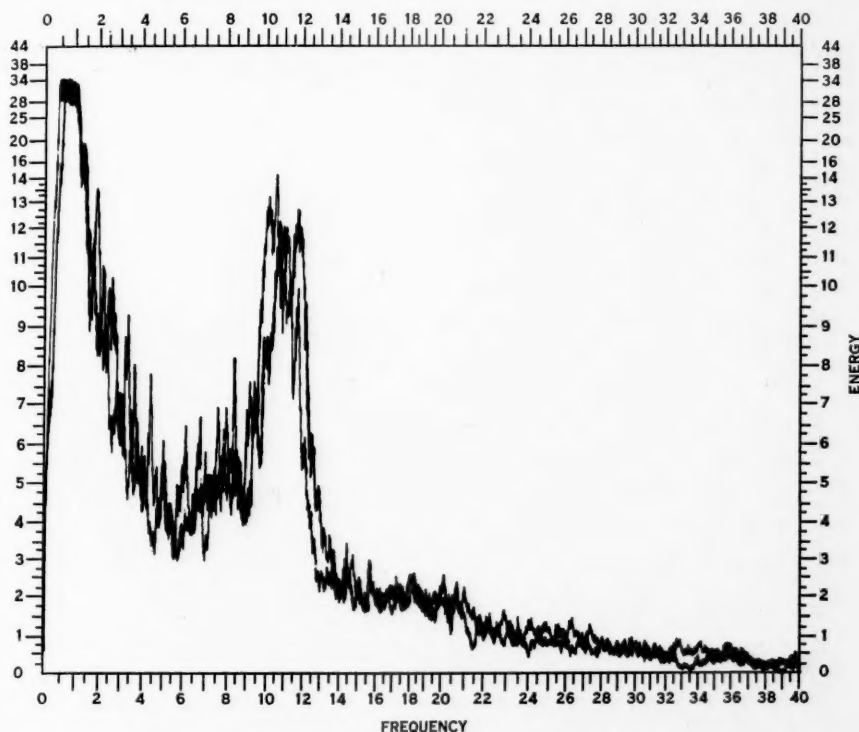


Fig. 1.—Typical shift in the cortical frequency spectrum to the slow side during pregnancy. *Black curve*, twelve days before term; *red curve*, one day post partum. Frequency is shown in cycles per second, and energy in arbitrary units that are convertible to millivolts. This is Case 4 in Table I. The spectra were made with a Grass analyzer from records of the electrical activity of the right occipital area.

Slow records occurred as commonly among patients with toxemias as among patients with a normal pregnancy (Table II). The difference between the two groups appears to lie in a greater incidence of high-voltage fast records among patients with toxemia and in a smaller incidence of perfectly normal records. In the one case of eclampsia that was studied, the record was obtained during stupor; the cortical activity at that time was extremely slow. In one case studied just before pregnancy was interrupted because of severe cardiac decompensation, the electroencephalogram was also slow.

TABLE I

CASE	PREPARTUM		POST PARTUM				CLINICAL DIAGNOSIS
	DAYS BEFORE DELIV- ERY	EEG	DAYS AFTER DELIV- ERY	EEG	DAYS AFTER DELIV- ERY	EEG	
1	2	9½/sec.	7	10/sec.			Normal pregnancy
2	1	11 /sec.	7	12/sec.			Normal pregnancy
3	1	11½/sec.	3	12/sec.			Normal pregnancy
4	12	10½/sec.	1	11/sec.			Normal pregnancy
5	10	Slow	1	9/sec.			Normal pregnancy
6	10	Slow	9	11½/sec.	67	11 ½/sec.	Normal pregnancy
7	10	9½/sec.	12	Low-V.* fast			Normal pregnancy
8	9	Slow	2	9½/sec.			Normal pregnancy
9	1	Slow	9	Very slow			Normal pregnancy
10	4	Very slow	5	Slow	55	Slow	Normal pregnancy
11	2	Slow	7	Slow			Normal pregnancy
12	1	Slow	10	Low-V.* fast			Normal pregnancy
13	5	9 /sec.	4	9½/sec.	60	9½/sec.	Mild pre-eclampsia
14	36	Slow	15	Low-V.* fast			Pre-eclampsia
15	1	High-V.* fast	20	High-V.* very fast	74	High-V.* very fast	Pre-eclampsia
16	2	Slow	9	8/sec.			Pre-eclampsia
17	90	Very slow	(Hys- terec- tomy)	Slow			Rheumatic heart

\*Voltage.

TABLE II

	SLOW	NORMAL	HIGH-V. FAST
Control (100 nonpregnant women)	8%	85%	7%
Normal pregnancy (20 cases)	40%	60%	0
Pregnancy with toxemia (8 cases)	40%	10%	50%

## DISCUSSION

Slow cortical activity and high-voltage fast activity are common in a variety of conditions associated with evidence of cerebral dysfunction.<sup>1</sup> All conditions in which the incidence of convulsions is higher than in the general population are associated with a high incidence of electroencephalograms that are classified as slow or high-voltage fast. Tonic-clonic convulsions are usually accompanied by an abnormal acceleration of cortical activity,<sup>2</sup> and grand mal seizures can be predicted in epileptics by an increase in the amount of fast activity.<sup>3, 4</sup> The occurrence of abnormally fast activity in half of the patients with pre-eclampsia suggests that in pre-eclampsia cortical activity is commonly in a subconvulsive state. Endocrine and metabolic factors are known to alter the electrical activity of the cortex,<sup>5-10</sup> but an increase in cortical frequency, such as occurs with an increase in metabolic rate, could not explain the present findings, nor would any known change in sugar metabolism. Detailed consideration of the factors that may be responsible for the



modification of cortical frequency in pregnancy will be deferred until more data are available.

#### SUMMARY AND CONCLUSIONS

An electroencephalographic study of 28 pregnant women, 8 of whom had pregnancy toxemias, indicates that the electrical activity of the cortex is slowed in pregnancy and that, as a group, patients with pregnancy toxemias show more high-voltage fast activity and less normal activity than patients without toxemia.

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#### CONVULSIONS FOLLOWING THE INTRAVENOUS ADMINISTRATION OF PITUITARY EXTRACT

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**A** THOROUGH survey of the literature concerning the use and abuse of posterior pituitary extract in obstetrics reveals that the vast majority of clinical and laboratory investigators condemn its indiscriminate use in the first stage of labor; sanction a judicious use in the second stage and generally laud its beneficent properties in the third stage. It is probably fair to assume that many obstetricians use pituitary extract without much consideration of the possible toxicology involved.

In 1933 the senior author<sup>1</sup> reported the intravenous use of the extract in 100 cases of cesarean section with uniformly good results and no toxic effects. In 1936 Pastore<sup>2</sup> reported on the use of the drug in the third stage of labor and in the control of post-partum hemorrhage, used intravenously, with one death due to shock. White,<sup>3</sup> in 1938, reported the intravenous use in 630 cases with no bad results. In 1940 Gardiner, Sprague, and Bradbury<sup>4</sup> found that the intravenous use of the drug was

attendant with no ill-effects. It is evident from the reports in the literature and the wide clinical use of the drug that toxic side-effects occur in a very small percentage of cases.

The posterior pituitary extract used in obstetrics is water soluble, purified to remove inert protein, and contains a pressor and oxytocic principle. Efforts have been made to separate the two, but it is generally accepted that any solution of one contains minute amounts of the other.<sup>5</sup> Three different varieties of toxic reactions following the use of pituitary have been noted. The first and most common is the reaction called pituitrin shock. It is characterized clinically by pallor, increased pulse rate and fall in blood pressure, headache with occasional abdominal pain, nausea and vomiting. These phenomena are caused by a generalized capillary vasoconstriction and the most alarming symptoms: pallor, rise in pulse rate and drop in blood pressure are due to coronary constriction with resultant anoxemia of the cardiac musculature, consequent vasodilatation and lessened cardiac output.<sup>6, 7</sup> A second type of pituitary reaction is one resembling true anaphylactic shock and is characterized by severe urticaria and a localized or general pruritus. Cases of patients have been reported with marked edema of the eyes, face, glottis, or lungs, with or without severe shock.<sup>8-10</sup> We have been unable to find what we believe to be a third type of toxic response, reported in American literature although cases have been reported from abroad. This third type is characterized by tetanic convulsions with either a rise or drop in blood pressure.

In 1915 Seifert<sup>11</sup> reported tinnitus, anxiety, albuminuria, unconsciousness, and convulsions following the use of posterior pituitary extract. In 1922 H. Vermelin<sup>12</sup> reports convulsions following the use of 1 c.c. of the extract in a previously normal primiparous parturient. In the same communication Van Cauwenberghe reported convulsions in a primipara seventeen hours after delivery, and Wegmeersch noted convulsions after the use of the drug. In 1927 Lawrence and Shackle<sup>13</sup> described convulsions in a multipara, occurring four days post partum just after the drug had been used for subinvolution. This case was complicated by a severe diabetes and brings to mind DeLee's<sup>15</sup> warning to be careful of the use of pituitary in diabetics and patients with thyroid dysfunction. In 1936 Schockaert,<sup>14</sup> of Brussels, published the same reaction in a primipara with a previously normal prenatal course.

A case of convulsions following the intravenous administration of 3 minims of pituitary extract is reported herewith.

Mrs. O., a 37-year-old primipara, was under prenatal supervision from June 14, 1941. There had been no serious illnesses and no operations. Her family history was significant in the light of subsequent events in that she had one sister who suffered from severe epileptic attacks. The catamenia had been normal and regular, and her last period began March 12, 1941, making her expected date of confinement Dec. 19, 1941. The general physical examination revealed no abnormalities, the blood pressure was 120/70, the examination of the urine disclosed no albumin

or sugar, and the sediment was negative. Her weight was 114 pounds. There was no evidence of endocrine imbalance. Throughout her pregnancy the urine remained free of albumin and her blood pressure was within normal limits. She was last seen in the office on Dec. 26, 1941 and at that time her blood pressure was 122/78, the urine was negative, and she weighed 137 pounds, the baby was large and the vertex was riding high. Because she was overdue, x-ray studies were made of her pelvis. These confirmed the impression of cephalopelvic disproportion, and she was booked for cesarean section. Early the following day the patient was admitted to the hospital with a history of ruptured membranes, slight show, and irregular, mild uterine contractions. A voided specimen at this time showed a slight trace of albumin, and on the nurse's chart was recorded the fact that the patient passed a large amount of urine at the time, although it was not measured. Throughout the morning the patient continued having mild uterine contractions. No medication was given. Immediately before the operation she stated that she felt fine and had no complaints. Her blood pressure at this time was 120/70. She received no preoperative medication, and at 11:15 A.M. spinal anesthesia was administered. The spinal needle was placed in the third lumbar space and 75 mg. of novocain crystals were mixed with 2 c.c. of spinal fluid and injected slowly. A skin wheal had been previously raised with a mixture of 1 per cent novocain and 50 mg. of ephedrine sulfate. Just before and for some time after the administration of the anesthesia the blood pressure was recorded at 130/70, and there was no immediate change following the injection of the anesthesia. The patient was placed in moderate Trendelenburg position fifteen minutes after the administration of the anesthesia. The blood pressure remained at the above-mentioned level, and there was no subjective complaint from the patient until after the administration of three minims of obstetric pituitrin. This was given intravenously in 4 c.c. of saline solution immediately after the removal of the baby through a low transverse cervical incision.

Immediately after the pituitary extract was given the patient developed a sharp pain in the chest in the region of the xiphoid process. Simultaneously she complained of a sharp pain in the head which localized in the occipital region. Shortly thereafter she became nauseated and regurgitated. The nausea and the vomiting subsided with the administration of oxygen, but the chest pain and headache persisted. The patient was given 1 ampoule of ergometrine intramuscularly after the delivery of the placenta. She was also given morphine sulfate, grain  $\frac{1}{6}$ , because of her complaint of headache and substernal pain. There was no sharp rise in blood pressure readings, but there was a steady trend upward beginning with the administration of the solution of pituitary extract, at which time it was 130/70, until the operation was concluded twenty-five minutes later when the recorded blood pressure was 150/80. Throughout the entire operation the pulse varied between 92 and 96. The patient was returned to her bed from the operating room and in thirty minutes her pressure was recorded at 210/110. The nurse's chart states that she was complaining bitterly of occipital headache and was very alert. The patient was given 3 gr. of nembutal and became drowsy.

For the next three hours her pressure varied between 210/110 and 188/100, and during this time her pulse varied from 84 to 100. Three hours after the administration of the pituitary extract and the onset of her symptoms, the patient had a generalized tetanic convulsion which lasted for one minute. Intravenous magnesium sulfate, dose 20 c.c. of

a 10 per cent solution, and sodium luminal, 5 gr., was administered intramuscularly. A catheter was introduced to the bladder and nine ounces of urine obtained; this specimen showed a large trace of albumin. In a period of five hours a total of 9 ounces of urine was excreted. Magnesium sulfate therapy was continued with a 25 per cent glucose solution on alternate hours plus sodium luminal sedation. During this period of seventeen hours her urinary output was 26 ounces and each specimen showed a large trace of albumin. During the same interval her blood pressure varied from 190/110 to 170/100. She was very drowsy but when she did respond she complained only of occipital headache.

Seventeen hours after the first convulsion a second fit occurred and this also lasted for one minute. Following the second convulsion the patient lost control of her sphincters and was placed on constant drainage. A lumbar puncture was then performed. The initial pressure was 210; this was reduced to fifty by the slow withdrawal of 20 c.c. of spinal fluid over a period of ten minutes. Examination of the fluid revealed one lymphocyte and numerous red blood cells. The spinal tap was easily performed and was believed to be atraumatic.

During the course of the next six hours, continuing with magnesium sulfate and glucose on alternate hours, the pressure dropped gradually and varied between 158/170 and 190/100. Paraldehyde was substituted for sodium luminal because the patient was restless. A second spinal tap was performed at the end of this six-hour period, and the pressure was found to be 70. Examination of the eye grounds at this time revealed no evidence of increased intracranial pressure. All medication with the exception of paraldehyde was stopped. At this time the blood pressure was 140/90. The patient was controlled on gradually decreasing doses of paraldehyde and the blood pressure dropped, with short exacerbations, until on the third postoperative day it was 120/70. Albumin gradually disappeared from the urine and on the third day it was absent. The urinary output on the second day was 55 ounces and on the third day was 87 ounces. The occipital headache disappeared after the second lumbar puncture and did not recur. The surgical wound healed well; there was no postoperative nausea or vomiting and no distention. The patient was out of bed on the eleventh and discharged on the fourteenth day post partum.

#### DISCUSSION

The point will be raised that the convulsions were the result of a fulminating post-partum eclampsia. We believe this may be ruled out by a consideration of the patient's past history and prenatal course which was entirely negative; also by our personal observations of the onset of the syndrome which immediately coincided with the intravenous administration of the extract. She was seen one day before operation at which time she was symptom free, and the blood pressure and urinary findings were normal. On the morning of admission to the hospital the patient voided a large quantity of urine as noted in the nurse's report. In this specimen there was a slight trace of albumin, but her membranes had ruptured and the urine was contaminated with amniotic fluid. There was no edema at any stage and a speedy return to normal without residua was made.



In 1895 Oliver and Schaefer<sup>16</sup> described a rise in blood pressure due to posterior pituitary extract and they ascribed this phenomena to a generalized vasoconstriction. They noted that this rise was particularly marked in the intravenous use of the substance. It is evident that individuals vary in their susceptibility and reaction to the drug. Moffat<sup>17</sup> studied the effect of pituitary extracts on the blood pressure in man and concluded that there was no constant rise but rather a tendency to drop after intramuscular use. In a few individuals there was a marked change but this was frequently a fall rather than a rise. In a study on the effects of posterior extract in pregnant women Dieckmann and Michels<sup>18</sup> noted that the magnitude of the vasomotor response did not bear a direct relationship to the size of the dose. This observation was confirmed by Dexter and Weiss<sup>19</sup> working on rabbits, who determined that the height of the peak rise in blood pressure and the duration of the same were not proportional to the dosage. Dieckmann and Michels, studying the effect on nonpregnant women, found a decrease in the volume of the urine with an increase in urinary chloride and little or no rise in blood pressure. In known pre-eclamptics they found the same results with the addition of a marked rise in blood pressure. De-Valera and Keller,<sup>20</sup> in England, made a comparable study with about the same results. In an investigation of nonpregnant and pregnant normal women, pre-eclamptics, and patients during the puerperium they found that the most marked response to posterior pituitary extract was obtained in the pre-eclamptic group, and this was followed by the nonpregnant and puerperal group with the least significant reaction obtained in the normal pregnant women who proved to be relatively insensitive to the drug. Our patient received ephedrine sulfate, 50 mg., with novocain when a skin wheal was raised for spinal puncture. This fact is important because of the work reported in 1931 by Melville and Stehle.<sup>21</sup> These investigators found that the vasopressin action of pituitary is enhanced when its use is preceded by adrenaline or ephedrine. The coronary dilating action of ephedrine thus eliminates the constricting action of the pituitrin with a consequent rise rather than a drop in blood pressure. In other words the nature of the blood pressure response to pituitary extract is determined by the extent and nature of the effect on the coronary vessels which, in our case, were dilated by the use of ephedrine and which probably remained so when the peripheral vessels were constricted by the pituitary extract resulting in a rise in pressure. This case presentation is also interesting in a consideration of the theories promulgated by Hofbauer<sup>22</sup> working experimentally with intravenous pituitary extract in dogs. Hofbauer was able to bring about changes which were similar to those found in the eclamptic state. These phenomena were hyperglycemia, increased lactic acid content, lowering of the CO<sub>2</sub> combining power, and an increase in inorganic phosphates. He postulated that in toxemia there was an excess of posterior pituitary substance which by its known pressor and antidiuretic action brought about a state of anoxemia in the tissues due to interference with oxygenation from angiospasm. Working along the same lines Anselmino and Hoffmann<sup>23</sup> reported an increased amount of posterior pituitary extract in the blood of patients with eclampsia. Teel and Reid<sup>24</sup> working at the Boston Lying-in Hospital have, in some cases, shown the presence of an antidiuretic substance in pre-eclamptics and eclamptics. These findings were not consistent in all cases but were found most often in those cases with pronounced edema. Kustner<sup>25</sup> also



reports an increase of posterior pituitary substance in the serum of an eclamptic patient. A number of workers, however, notably Byrom and Wilson<sup>26</sup> and more recently Dexter and Weiss<sup>19</sup> were unable to duplicate the results of the above workers. In consideration of the present case, the observation of Keith, Freidman and Barbour<sup>27</sup> is interesting. These men found that the presence of posterior pituitary extract in the cerebrospinal fluid stimulated the cerebral vasomotor centers, causing a prolonged rise in blood pressure. The cerebral arteries were constricted causing a cerebral anoxemia. This in turn favors increased capillary permeability with perivascular exudation, edema of the brain, and increased intracranial pressure.

Our patient's past history was negative for any sign of cerebral sensitivity, but there is a familial history of epilepsy and the question of cerebral dyskinesia might arise in seeking an explanation of her response. It is to be hoped that this presentation will stimulate the publication of any similar reactions which may have been observed. Since this unfortunate incident occurred, the authors have used an intravenous ergot preparation instead of pituitary extract.

#### SUMMARY

A case of post-partum convulsions in an apparently nontoxic parturient patient following the intravenous administration of three minims of pituitary extract is recorded.

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# THE TREATMENT OF PELVIC INFLAMMATORY DISEASE WITH INTRADERMAL ADMINISTRATION OF BACILLUS COLI VACCINE

## A SUPPLEMENTARY REPORT

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IN THIS paper 228 additional cases of pelvic inflammatory disease of puerperal and venereal etiology are presented. All were treated by intradermal injections of a vaccine of *B. coli* which contained 3 billion organisms per cubic centimeter. Supplementary operative procedures were performed as they were indicated. The new cases were followed for an average of 7.1 months.

Tables I to X present interesting data in regard to this new material and the old series of 172 cases that were reported in this JOURNAL, January, 1941. Specific details of treatment may be found in that article.

This study led to the following conclusions:

1. Intradermal administration of a suitable and potent foreign protein substance, such as our vaccine, was effective treatment. It was more safe and less uncomfortable to the patient.
2. Adequate medical treatment deserved a trial before resorting to radical surgery in every case.
3. Expertness in diagnosis and judgment in treatment improved with experience.

TABLE I. AGE AND COLOR DISTRIBUTION (400 CASES)

	WHITE	BLACK	TOTAL
10-15 yr.	2	0	2
16-20 yr.	26	52	78
21-25 yr.	48	90	138
26-30 yr.	29	44	73
31-35 yr.	23	24	47
36-40 yr.	7	12	19
41-45 yr.	3	5	8
46-50 yr.	0	2	2
Over 50 yr.	2	2	4
No record	12	17	29
Total	152	248	400

Table I presents the age and color distribution of our patients. All were indigent and were treated at the out-patient department at Receiving Hospital.

Approximately one-fourth of our patients were admitted to the hospital prior to treatment in the dispensary because of their "acute condition." Those designated as having had "no treatment" received bed rest, cold to abdomen, and sedation; they were discharged in a few days. The cases designated as "treatment" received in addition to

that mentioned above, parenteral fluids, blood transfusions, foreign protein, drainage of abscess, etc.; their hospital stay ranged from one to several weeks (Table II).

TABLE II. CASES ADMITTED TO HOSPITAL PRIOR TO TREATMENT IN O.P.D.

	OLD SERIES	NEW SERIES	TOTAL
No treatment	42	26	68
Treatment	19	18	37
Total	61	44	105

TABLE III. NUMBER OF COURSES OF VACCINE (SIX INJECTIONS) GIVEN EACH CASE

COURSES	OLD SERIES	NEW SERIES	TOTAL
Less than one	8	17	25
One	122	177	299
Two	35	28	63
Three	5	5	10
Four	1	1	2
Five	1	0	1
Total	172	228	400

Table III presents the number of courses of vaccine that were given to the patients. The majority of our cases (81 per cent) required one course of vaccine or less. An attempt was made to analyze those cases requiring more than one course of treatment and to discover a possible reason for extended treatment. An active infection of the cervix was the most outstanding reason. The need for further treatment and the presence of complications such as phlebitis, hemorrhage, pyelitis, abscess, etc., followed in order (Tables IV and V).

TABLE IV. COMPLICATIONS PRESENT WHEN TWO OR MORE SERIES OF VACCINES WERE GIVEN (400 CASES)

COMPLICATIONS	NUMBER	PER CENT
Required treatment	26	6.5
Chronic cervicitis	30	7.5
Complications, pyelitis, etc.	7	3.5
Hospitalization advised	3	
Irregular treatment	2	
No treatment necessary	1	
Trichomonas vaginalis	1	

TABLE V. COMPLICATIONS PRESENT WHEN THREE OR MORE SERIES OF VACCINES WERE GIVEN (400 CASES)

COMPLICATIONS	NUMBER
Required treatment	2
Chronic cervicitis	9
Complications, pyelitis, etc.	1

Table VI presents the number of months of treatment that were given to the patients. The majority of our cases (75.5 per cent) required one month, or less, of treatment. Tables VII and VIII attempt to analyze the reasons that prolonged treatment beyond one month. Again the outstanding reason was the presence of an active chronic cervicitis; slow response to treatment was next.

TABLE VI. NUMBER OF MONTHS OVER WHICH VACCINE WAS GIVEN

MONTHS	"OLD" SERIES	"NEW" SERIES	TOTAL	PER CENT
Less than one	3	6	9	75.5
One	118	175	293	
Two	27	20	47	
Three	10	10	20	
Four	3	3	6	
Five	2	0	2	24.5
Six	3	5	8	
Seven	3	5	8	
Eight	0	3	3	
Nine	1	0	1	
Twelve	0	1	1	
Fifteen	1	0	1	
Forty-two	1	0	1	
Total	172	228	400	

TABLE VII. COMPLICATIONS PRESENT WHEN PATIENTS REQUIRED MORE THAN TWO MONTHS OF TREATMENT (400 CASES)

COMPLICATIONS	NUMBER
Required treatment	11
Chronic cervicitis	25
Posterior colpotomy	5
Uterine retroversion	1
Salpingectomy done	2
Hemorrhage	1

TABLE VIII. COMPLICATIONS PRESENT WHEN PATIENTS REQUIRED MORE THAN THREE MONTHS OF TREATMENT (400 CASES)

COMPLICATIONS	NUMBER
Required treatment	7
Chronic cervicitis	15
Posterior colpotomy	5
Hemorrhage	1

TABLE IX. RESULT OBTAINED FROM VACCINE ALONE

	"OLD" SERIES	"NEW" SERIES	TOTAL	PER CENT
Cured	133	158	291	72.75
Improved	35	59	94	23.50
Unimproved	4	11	15	3.75
Totals	172	228	400	100.00

TABLE X. OPERATIVE PROCEDURES IN 400 CASES

	"OLD" SERIES	"NEW" SERIES	TOTAL	PER CENT
Posterior colpotomy	12	4	16	4.7
Other abscesses	3	0	3	
Polyps removed	0	3	3	
Conization	12	9	21	10.0
Cautery	12	6	18	
Sturmdorf	0	1	1	
Abdominal sections				
1. Performed	7	10	17	4.25
2. Refused	3	4	7	1.75
Totals	49	37	86	

Table IX presents the result obtained by the administration of vaccine alone.

Table X presents the 86 patients that were operated upon following the administration of vaccine therapy. Approximately one-half required the removal of cervical infection to effect a cure; 25 per cent required the drainage of an abscess; the remainder were advised to have abdominal section. Seven patients refused abdominal section because of the disappearance of subjective symptoms even though definite masses could be demonstrated. In the entire series of 400 cases, 6 per cent were advised to have abdominal section but only 4.25 per cent were actually operated upon.

I wish to express my deepest appreciation to my confreres in the clinic, Drs. R. Baer, D. M. Davidow, and F. B. Wight, who carried on the work when they took over the service; to Dr. H. Dibble, who, in the early stages of this investigation, kindly allowed me the use of his in-patient service; to Dr. D. M. Morrill, superintendent, who expedited the handling of case histories by supplying special forms; to Irene Weed who kept such excellent records; and last but not least all of those on the resident staff who did much of the actual detail.

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### ESTROGEN-WITHDRAWAL BLEEDING

#### A STUDY OF COMPARATIVE ACTIVITY OF VARIOUS ESTROGENS

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**T**HERE are numerous methods of comparing the relative value of the various estrogenic hormone preparations available commercially. Any evaluation of potency which is dependent on subjective response of the patient is, for obvious reasons, open to criticism. It is not within the province of this case report to discuss the relative merits of any of the usual procedures.

One fairly constant method of studying the response of a patient to estrogens is to produce an estrin-withdrawal type of bleeding. It is recognized that if estrogenic hormone be administered to a castrate whose uterus has been preserved, bleeding will follow regularly after cessation of administering the hormone, provided sufficient estrogen has been given. This method eliminates the subjective response entirely.

This report is concerned with the studies of a surgical castrate over a period of nearly four years. Various estrogens have been administered and evaluated entirely on the objective basis of producing estrin-withdrawal bleeding.

Mrs. G. G., white, 34 years of age.

*Past History:* Pregnancy, in 1936, was complicated by exacerbation of rheumatic fever. Normal baby was born May 9, 1936. In 1938, bilateral cystic ovaries were noted. Operation was performed July 23, 1938. Bilateral pseudomucinous cysts were removed. The postoperative course was uneventful. Within two months after operation, flushes were first noted. Subsequently she noted a fairly constant syndrome of head-



TABLE I

PREPARATION USED	DAILY DOSE	NO. OF DAYS OF TREATMENT	TOTAL MG. OF MEDICATION	RESULTS	
				OBJECTIVE	SUBJECTIVE
Stilbestrol (oral)	1.0 mg.	10 days	10.0 mg.	No bleeding	No improvement
Stilbestrol (oral)	4.0 mg.	13 days	52.0 mg.	Bleeding 5 days after cessation	Severe nausea
Stilbestrol (intra M)	5.0 mg. every other day	6 days	15.0 mg.	No bleeding	Nausea
Mixed estrogens* (intra M)	10,000 I.U. every 4th day	10 days	40,000 I.U.	No bleeding	Good
Mixed estrogens* (intra M)	15,000 I.U. 1 x week	48 days	110,000 I.U.	No bleeding	Fair
Mixed estrogens† (oral)	18,000 I.U.	20 days	360,000 I.U.	Good flow 7 days after cessation	Poor
Alpha estradiol (oral)	1.5 mg.	20 days	30.0 mg.	Cramps. No bleeding	Good
Alpha estradiol (oral)	2.0 mg.	16 days	32.0 mg.	Cramps. No bleeding	Good
Alpha estradiol (oral)	3.0 mg.	21 days	63.0 mg.	Flowed 6 days after cessation. Flowed 5 days	Excellent
Alpha estradiol (oral)	3.0 mg.	21 days	63.0 mg.	Flowed 5 days after cessation	Excellent
Alpha estradiol (oral)	3.0 mg.	14 days	42.0 mg.	Sl. brownish stain 5 days after cessation	Good
Alpha estradiol (oral)	2.5 mg.	21 days	52.5 mg.	Scant flow 6 days after cessation	Good
Alpha estradiol (oral)	2.5 mg.	21 days	52.5 mg.	Brownish stain 5 days after cessation	Fair
Alpha estradiol (oral)	3.0 mg.	21 days	63.0 mg.	Spotty flow 7 days after cessation	Excellent
Alpha estradiol (oral)	2.5 mg.	20 days	50.0 mg.	Flow 4 days after cessation	Good
Alpha estradiol (oral)	2.5 mg.	20 days	50.0 mg.	Flow 7 days after cessation	
Alpha estradiol (oral)	1.5 mg.	20 days	32.5 mg.	Brownish stain	Poor
Alpha estradiol (oral)	1.5 to 2.0 mg.	20 days	37.5 mg.	No flow	
Alpha estradiol in propylene glycol (sublingual)	0.5 mg. (1.0 c.c.) plus	21 days	12.5 mg. (25 c.c.)	3 days after cessation—cramps	Not as good as to oral
Ethinyl estradiol (oral)	0.1 mg.	6 days	0.6 mg.	No bleeding	Severe nausea and vomiting
Ethinyl estradiol (oral)	0.05 mg.	21 days	0.85 mg.	Good flow 7 days cessation	Excellent but bloated; nausea
Ethinyl estradiol (oral)	0.05 mg. q other day	21 days	0.45 mg.	No flow	Fair
Ethinyl estradiol (oral)	0.05 mg.	21 days	0.65 mg.	Good flow 6 days after cessation	Headache Nausea

\*Amniotin, Estrolin.

†Urestrin, Upjohn (estrogenic hormone, oral).

ache, tightness in the ears, weakness, and flushes. From October, 1938, to April, 1939, the patient received intermittent injections of various commercially available estrogens with varying subjective response. Since April, 1939, treatment consisted of oral administration of estrogens.

Table I reveals the detailed observations of type of medication, dosage, duration of treatment, and response during the past three years.

Above a certain minimum, there does not seem to be such a close relationship in this patient between an increase in amount of medication and the subjective response.

The subjective response to stilbestrol was very unsatisfactory. It has been our general observation that 1 mg. is sufficient to control the average menopausal syndrome. In this patient such was not the case, and when the dose of stilbestrol was raised sufficiently to result in bleeding upon withdrawal, severe nausea resulted.

The response to alpha estradiol was most constant. When the total dosage over a three weeks' period was less than 50.0 mg., the subjective response was uniformly poor, although a scant bloody flow might ensue. With dosage about 50.0 mg. in three weeks, the sense of well-being was best and the flow on withdrawal was best.

Alpha estradiol administered sublingually in solution in propylene glycol seemed to be about three to four times as potent as when taken by mouth in tablet form.

Ethinyl estradiol has proved to be the most active estrogen studied in this series. Using withdrawal bleeding as a criterion of activity, ethinyl estradiol is approximately fifty to seventy-five times as active as alpha estradiol, both administered orally.

The doses which controlled the menopause syndrome best subjectively were those which produce estrin-withdrawal bleeding.

#### CONCLUSIONS

1. Estrogen-withdrawal bleeding may be employed as an index of objective response to estrogen therapy.
2. Using estrogen-withdrawal bleeding as a criterion of activity, stilbestrol, estriol, alpha estradiol tablets, alpha estradiol in solution in propylene glycol and ethinyl estradiol were administered to a patient who had both ovaries removed surgically.
3. Ethinyl estradiol was the most active estrogen used. Alpha estradiol in propylene glycol, sublingual, was the next most active. Alpha estradiol, estriol and stilbestrol were of about equal potency in the dosage administered orally.
4. The best subjective response was obtained with maximum doses of alpha estradiol, and with minimal doses of ethinyl estradiol.

The alpha estradiol and ethinyl estradiol used in this study were supplied by Dr. Max Gilbert of the Schering corporation.

## VARIATIONS IN THE ELECTROENCEPHALOGRAM DURING THE MENSTRUAL CYCLE\*

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WHILE studying the correlation between brain potentials and other variables, such as heart rate, blood pressure, and metabolic rate, Lindsley and Rubenstein<sup>1</sup> found that in four cases the alpha frequency varied greatly during the midmenstrual period. They did not report, however, that there is a relation between brain potentials and the menstrual cycle. The present study was undertaken because such a relation seemed possible. This possibility was strengthened by the observation of Irving, Reid and Gibbs<sup>2</sup> that the electrical activity of the cerebral cortex is slowed during pregnancy.

### MATERIAL AND METHOD

Daily electroencephalograms of 11 healthy young women were obtained during at least one menstrual cycle. The activity of the right frontal, parietal, and occipital areas (indifferent electrodes on the ear) was recorded with a three-channel Grass electroencephalograph. At the same time, the activity of the right occipital area was recorded as a shadowgram on film. A strip of this shadowgram, thirty seconds in duration, was analyzed into a spectrum with the Grass frequency analyzer.<sup>3</sup>

### RESULTS

Day-to-day variations in the electrical activity of the cortex occurred in all cases. Changes were evident in the ink record, but they were most easily demonstrated in the spectra. Therefore, the data presented here are based entirely on successive-day comparisons of spectra. Each column in Figs. 1 and 2 represents a change in frequency from the preceding day. These deviations in frequency were determined as follows: The spectrum for a given day was placed on a transilluminator and the spectrum for the succeeding day laid over it. The attempt was made to obtain a maximal superimposition of the two curves by a displacement on the frequency scale. For example, if it was found after trial that when the curve for the succeeding day was shifted one-half cycle to the fast side, a maximal superimposition of the two curves was obtained, then the change was reported as a deviation of +0.5 cycle per record. In order to reduce the error introduced by subjective factors, spectra were compared by three observers independently without knowledge of

\*This study was aided by grants from the John and Mary R. Markle and the Rockefeller Foundations. Spectrum analysis was carried out with the aid of the Work Projects Administration under Official Project No. 165-2-00-3.

the date of menstruation. A deviation was recorded only when all three observers agreed on its occurrence and on its direction. The average of the deviations reported by the three observers was used in the final plot (Figs. 1 and 2). In Cases 6, 8, and 9, days were skipped; the omitted days are indicated by a break in the base line (Figs. 1 and 2). The record of the day after the day omitted was compared with the record of the day before the day omitted.

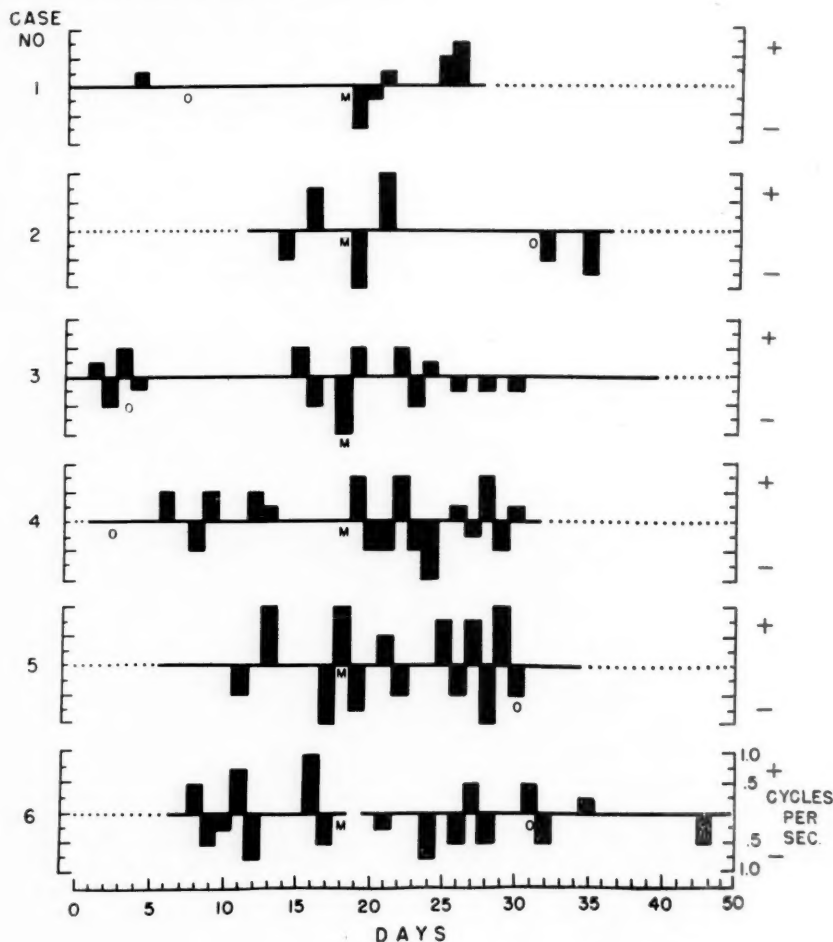


Fig. 1.

Figs. 1 and 2.—Variations in the frequency of cortical activity during the menstrual cycle. Columns show deviation of frequency from preceding day, based on comparison of right occipital spectra (see text). *M*, start of menstruation; *O*, mid-menstrual day, presumed to be close to ovulation. Gap in Cases 6, 8, and 9 indicates a day which was omitted.

Inspection of these figures reveals the following:

1. Shifts in frequency of the order of  $\frac{1}{4}$  to 1 cycle per second were demonstrable in all cases over a twenty-four-hour period.
2. The timing and magnitude of these shifts suggested a relationship to the menstrual cycle in seven of the 11 cases (Cases 1 to 6 and 10).

3. The onset of menstruation was followed by slowing in nine out of 11 cases (all cases except 3 and 4).

4. Shifts in frequency possibly related to ovulation occurred in the mid-menstrual period in eight of 11 cases (Cases 1, 2, 3, 5, 7, 8, 10 and 11). In 7 of the 11 cases, slowing occurred on either the midmenstrual day or the day after the midmenstrual day (Cases 2, 3, 5, 6, 7, 9 and 11).

#### DISCUSSION

These findings do not indicate a simple, rigid relation between the menstrual cycle and the electrical activity of the cortex, but they do indicate that sufficient slowing can occur in association with menstruation to change a normal electroencephalogram to an abnormal one. Differences in frequency of one-half cycle are significant. Such differences have been correlated with differences in behavior (4, 5, 6).

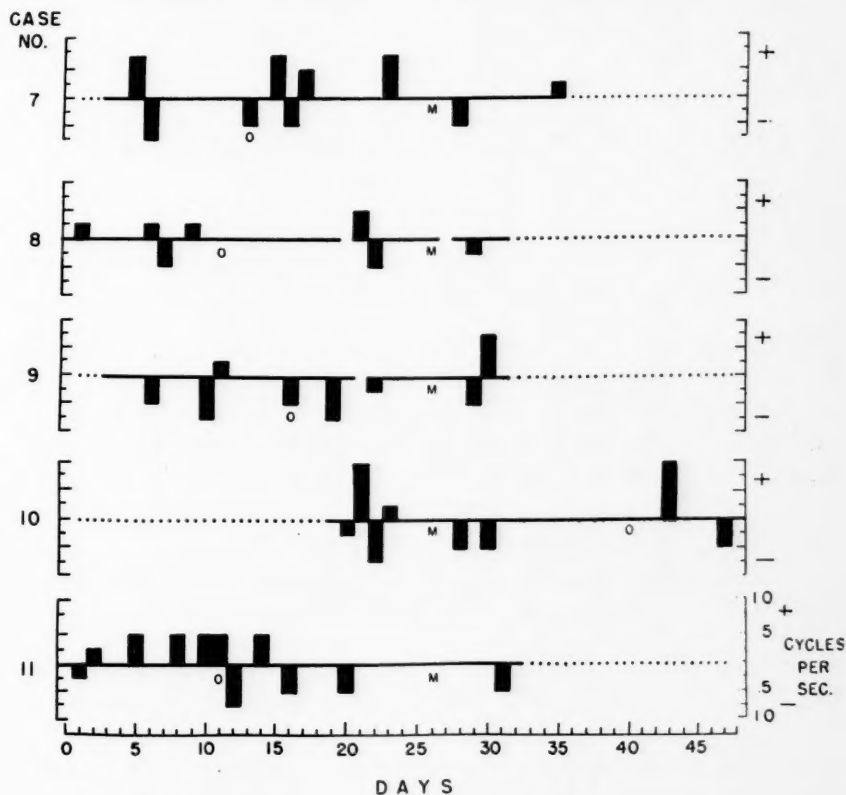


Fig. 2.

In view of these findings it seems reasonable to suppose that the changes in mood and efficiency commonly associated with the menstrual period may be related to modifications of central nervous function, modifications which may also manifest themselves in a change in the electrical activity of the cortex.



## SUMMARY AND CONCLUSIONS

Successive-day comparisons of the electrical activity of the cortex of 11 healthy young women revealed no simple rigid relation between the electrical activity of the cortex and the menstrual cycle, but in the majority of women this activity becomes slower after the beginning of the menstrual flow, and in some a disturbance in frequency regulation occurs at the midmenstrual period.

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### THE COLOSTRUM TEST FOR PREGNANCY IN A PRENATAL CLINIC

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THE colostrum test has created so much discussion since the original paper by Falls, Frieda, and Cohen in this JOURNAL (41: 431, 1941), that we decided to try it out in the prenatal clinic at the Harlem Hospital in New York City. Because no mention was made of the reactions in the colored as compared with the white race, we felt that this study would bring out interesting results. The only prerequisite was registration in the prenatal clinic.

Although this series was started in July, 1941, we waited until all of the patients could be checked clinically for a definite diagnosis before submitting our results.

Previous to the publication of our paper, Goldman, Kessler and Wilder, at the Newark Beth Israel Hospital, reported a series of cases in the *Journal of the American Medical Association* (119: 130, 1942). They followed the procedure of study of the original authors (Falls, Frieda, and Cohen), while we confined ourselves exclusively to patients attending the prenatal clinic.

We followed the original authors' technique with one exception. To rule out the possibility of a reaction to the merthiolate, we added a solution of merthiolate to both the colostrum and the saline control. We were rewarded for this precaution by having two cases that gave us a definite positive reaction to both the colostrum and the saline control. To eliminate further the possibility of error, all injections were

done by one of us. One-fiftieth of 1 c.c. of a solution of equal parts of human colostrum and saline was injected intradermally in the volar surface of the forearm.

We divided our results into three groups as follows:

- Group "A": Patients who gave a definite negative reaction to colostrum.  
 Group "B": Patients who gave a definite positive reaction to colostrum.  
 Group "C": Patients with a doubtful reaction.

A reaction was considered negative if there was no areola or a very slight areola and no wheal or a wheal smaller than in the original injection. A reaction was considered positive if there was an areola one inch or larger, a wheal larger than the original injection and pseudopods.

The size of the wheal was not consistent except in the definitely negative reaction group. Some of our positive results not only had a larger wheal than the originally described reaction together with pseudopods and an areola of at least one inch in diameter but also a much larger area of edema underlying and surrounding the entire site of injection.

It is our opinion that the size and intensity of the areola should be the primary determining factor in the reading of the results.

We classified our results under the headings of age, color, gravida, parity, Wassermann reaction, trimester of pregnancy, and any medical or surgical complications. We are wholly in agreement with the original authors in that none of these seems to have any bearing on the result.

#### RESULTS

*Group "A".*—Those with a definite negative reaction, i.e., pregnant:

	Total number	143
1. Total number correct diagnoses		130
2. Total number incorrect diagnoses		3
3. Total number of whom we lost track or could not establish a definite diagnosis		10

If we eliminate Group 3 in our calculations, we find that we have a correct diagnosis of 97.7 per cent and an incorrect diagnosis of 2.3 per cent in this group.

*Group "B".*—Those with a definite positive reaction, i.e., nonpregnant:

	Total number	16
1. Total number correct diagnoses		4
2. Total number incorrect diagnoses		12

In this group we find 25 per cent correct and 75 per cent incorrect diagnoses.

*Group "C".*—Those giving a doubtful reaction.

Here the areola was pale, less than one inch in diameter and either did or did not have a suggestion of pseudopods. Due to the great number that gave such a reaction, we felt that charting them merely as doubtful or inconclusive would eliminate a great number of cases from our series.

Therefore we considered these as negative in our final computations:

Total number	61
1. Total number correct diagnoses	55
2. Total number incorrect diagnoses	2
3. Total number not checked	4

Eliminating Group 3, we get 96.5 per cent correct diagnoses and 3.5 per cent incorrect diagnoses.

Adding Group "A" and Group "C" we have the following:

Total number of negative results	190
Total number of correct diagnoses	185
Total number of incorrect diagnoses	5

Thus we may conclude that if we get a definitely negative result as in Group "A" or a doubtful reaction as described in Group "C," we have 97.4 per cent correct diagnoses for pregnancy and 2.6 per cent incorrect diagnoses.

In this series there were 197 definitely pregnant women in whom the colostrum gave a correct diagnosis in 94 per cent and an incorrect diagnosis in 6 per cent. There were also 9 nonpregnant women in whom we made a correct diagnosis with colostrum in 44 per cent and a wrong diagnosis in 56 per cent.

Thus we find that in a negative reaction to the colostrum, the test will be correct as a positive diagnosis of pregnancy in 97.4 per cent of the cases. On the other hand, a positive reaction to the colostrum is only 25 per cent reliable in making a diagnosis of nonpregnancy. Whereas pregnant patients will give a correct reaction to the colostrum in 94 per cent of the cases, nonpregnant ones will react correctly in only 44 per cent of the cases. Therefore, we must admit that the test is of definite value when we get a negative reading and of no value where the result is positive.

We had occasion to use the Friedman modification of the Aschheim-Zondek test for a check in 13 cases. Our results are tabulated in Table I.

TABLE I

COLOSTRUM TEST				ASCHHEIM-ZONDEK TEST			
NO.	DATE	READ- ING	RESULT	DATE	READ- ING	RESULT	CLINICAL DIAGNOSIS
217	12/19/41	Neg.	Correct	11/25/41	Neg.	Wrong	Pregnant 2 months
				12/26/41	Pos.	Correct	
187	12/ 4/41	Pos.	Correct	12/ 1/41	Neg.	Correct	Amenorrhea 5 months
216	12/16/41	Neg.	Wrong	10/27/41	Neg.	Correct	Amenorrhea 8 months
158	11/25/41	Pos.	Correct	10/31/41	Neg.	Correct	Sterility 10 years
177	11/28/41	Neg.	Wrong	11/28/41	Neg.	Correct	Amenorrhea 9 months
183	11/28/41	Neg.	Correct	10/29/41	Pos.	Correct	Pregnant 5 months
146	10/27/41	Pos.	Correct	10/30/41	Neg.	Correct	Amenorrhea 3 months
152	11/21/41	Neg.	Correct	10/ 4/41	Pos.	Correct	Pregnant 5 months
115	10/20/41	Pos.	Correct	10/28/41	Neg.	Correct	Amenorrhea 2 months
91	8/15/41	Neg.	Correct	2/ 6/41	Pos.	Correct	Pregnant
102	9/ 7/41	Pos.	Wrong	9/26/41	Neg.	Wrong	Threatened abortion
37	7/22/41	Neg.	Wrong	10/16/41	Neg.	Correct	Amenorrhea. Bilateral salpingectomy
							Pituitary disease
29	7/18/41	Neg.	Wrong	2/15/41	Pos.	Wrong	
				5/26/41	Neg.	Correct	

In view of the fact that Cases 217 and 29 gave two contradictory Aschheim-Zondek reports, we eliminated them in our final calculations.

Thus in our small series of 11 cases where a clinical diagnosis could not be made, the colostrum test was correct in 7 (63.6 per cent) and wrong in 4 (36.4 per cent).

The Aschheim-Zondek test was correct in 10 (90.1 per cent) and wrong in 1 (9.9 per cent).

Even in this small series the tremendous advantages of the Aschheim-Zondek test over the colostrum test are very amply illustrated.

#### DISCUSSION

In this series we made readings at fifteen minutes, thirty minutes, and one hour. We found that many reactions were indefinite in the first half hour and then became either definitely positive or negative. We found it therefore more advantageous to take our final reading at the end of one hour.

The technique of the test is simple but from our experience the interpretation is difficult. Falls, Frieda, and Cohen read their results as positive, negative, and doubtful. Goldman, Kessler, and Wilder divided them into one-plus, two-plus, three-plus, and four-plus. They called all reactions above two-plus positive. In this series we listed them as positive if the areola was over one inch in diameter and negative if there was no reaction or a very slight one. We considered the doubtful cases as negative. This may account for the high percentage of correct diagnoses in the group of negative reactions.

Although it is very simple to read a definite negative reaction or a definite positive reaction, so many gave a doubtful reaction (61) that a fair amount of experience is needed to differentiate between a positive and a doubtful reaction. One of the disadvantages of the colostrum test, therefore, is the difficulty of interpreting the final reaction.

It was our purpose in this paper to attack this problem from a clinical point of view and from the point of view of the general practitioner who in the last analysis still diagnoses and treats the vast majority of pregnant women.

#### CONCLUSIONS

1. A negative reaction is 97.4 per cent accurate in diagnosing actual pregnancy.
2. A positive reaction is 75 per cent incorrect in the diagnosis of non-pregnancy.
3. In pregnant women the colostrum test will give a correct (negative) reaction in 94 per cent of the cases.
4. In nonpregnant women the test is 56 per cent wrong.
5. The test lacks the accuracy and reliability of the Aschheim-Zondek test in doubtful cases.
6. It would be misleading to consider a positive reaction as either definite or presumptive evidence of the nonpregnant state.

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## UTERINE TONUS DURING LABOR

### TOCOGRAPHIC OBSERVATIONS UPON A PATIENT EXPERIENCING ABRUPTION OF THE PLACENTA

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**R**ECENTLY we registered the uterine contractions of a series of patients at frequent intervals throughout labor with a Lóránd tocograph. One patient experienced an abruption of the placenta. The unusual character of this individual's tracing seemed to warrant its being placed on record.

#### CASE REPORT

Patient A. M., colored, aged 37 years, para xi, received prenatal care from the thirtieth week of gestation onward. Previous to this pregnancy she had experienced a mild hypertension. On her first clinic visit, her blood pressure was 140/96. One week before admission, however, it was only 110/80.

At the fortieth week of pregnancy, she was admitted to the hospital with a history that vaginal bleeding had started forty-five minutes earlier. She had felt no fetal movements following the onset of bleeding. Examination revealed signs of incipient shock; the blood pressure was 90/70; hemoglobin, 72 per cent; and urine showed 3+ albumin. The uterus was tense, and fetal heart sounds were absent. There was a slight trickle of blood coming from the vagina. The cervix was 3 cm. dilated and one-half effaced, and the membranes were intact. No placental tissue could be felt within 3 cm. of the internal os.

The membranes were punctured. Seven and one-half hours after the amniotic fluid was drained away, a stillborn infant, weighing 3,200 Gm., was delivered spontaneously. The placenta and about 1,000 c.c. of clotted blood were expelled immediately. Following this, some slight bleeding continued, and the patient soon went into severe shock. In spite of applying the usual measures, including transfusion, the patient died within one hour of delivery. Post-mortem examination revealed a large flabby uterus with a rupture 3 cm. in length in the right side of the lower uterine segment, and an extensive subserosal suffusion of blood extending along the distribution of the large uterine vessels. There was no bleeding into the abdominal cavity.

The tocographic tracings are reproduced in Fig. 1, where their timing in relation to the labor is noted. Each tracing begins at the left. The tocograph was placed upon the patient at "a" where the graph leaves the base line, and removed at "b". Tracing 1 was of thirty-three minutes' duration. The horizontal line above each graph marks the highest point to which it can rise.

#### COMMENT

We were fortunate, in this case, to secure records of uterine activity which covered practically the entire period from the time that the abrup-



tion occurred until delivery took place. The opportunity to secure such a series of tracings was exceptional, since we had on hand a team of nurses trained in tocographic recording, and also since the conditions met with in connection with this accident of labor usually are such that cesarean section is performed.

The points of special interest in this case are four: (1) The type of uterine activity associated with abruption of the placenta. (2) The influence of the draining away of the amniotic fluid upon uterine tonus. (3) The influence of the type of activity upon the progress of labor. (4) What is meant by the term "tonus"?

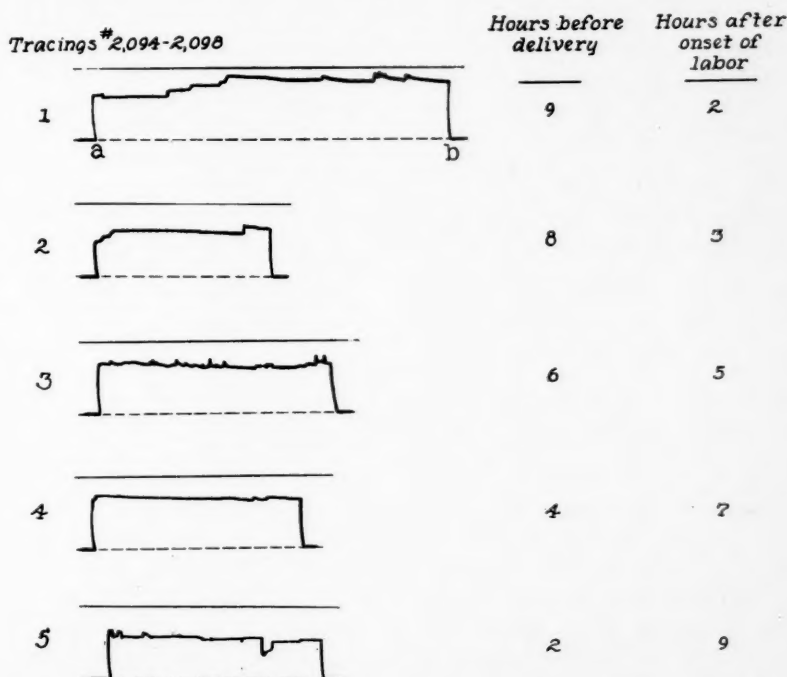


Fig. 1.—Tocographic record of uterine activity of patient suffering from abruption of the placenta. All tracings secured between first signs of abruption and delivery of infant. Tracing begins when tocograph is placed upon patient's abdomen at "a" and ends when it is removed at "b." Note immediate elevation of graph from base line as tocograph is placed in position for recording. This distance is the measure of tonus. Tracing 1 was completed in thirty-three minutes. Note high tonus in all tracings and total absence of intermittent contractions of significant size. Compare tracings of Fig. 1 with Fig. 2. Note lower tonus and the presence of contraction waves in Fig. 2.

*Type of Uterine Activity.*—The chief point of interest in the tocographic tracings of this patient lies in the fact that none of them recorded any evidence of the intermittent contractions which occur so frequently both during late pregnancy and in normal labor. The patient's abdomen was extremely tense at all times before delivery, and this characteristic seems to have been graphically recorded by the tocograph. The type of activity exhibited by the present patient is seen more clearly when compared with a tracing of another patient (Fig. 2) who experienced a normal labor. These findings show how the tocograph may be employed for the purpose of making available a more detailed picture of what is

going on in the uterus than can be gathered from simple physical examination of the abdomen.

*Influence of Draining Away of Amniotic Fluid Upon Uterine Activity.*—The membranes were punctured twenty-seven minutes after Tracing 1, Fig. 1 was begun, and eighteen minutes before Tracing 2 was started. No significant drop in tonus followed this operation. The lowering of tonus observed in Tracing 2 was of only slight and temporary nature; this decrease may have been more apparent than real, since the tocograph was removed from the patient before the membranes were punctured. The membranes have ruptured spontaneously during the taking of tocographic tracings of a number of other patients, and this has had no significant effect upon their graphic records.

*Relation of Type of Activity to the Progress of Labor.*—Although the present patient experienced no significant intermittent contractions while any of the tracings were being made; nevertheless, her cervix effaced and dilated. This experience raises the question as to whether the contractions are necessary for the opening of the cervix. Perhaps, they do not play as important a role in this connection as we have assumed in the past. The question requires further study, but the present observations suggest that the intermittent contractions are not necessary.

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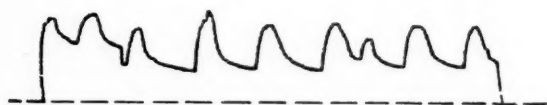


Fig. 2.—Tocographic record of uterine activity of patient who experienced normal labor. Compare with Fig. 1.

*Definition of the Term Tonus.*—Students of uterine motility, unfamiliar with tocographic recording, raise the question as to just what is being measured by the distance of the graph above the base line. Does it represent faulty technique, distention by the uterine contents, or actually the tenseness of the uterus?

What we term tonus does not appear to be due to the tightness of the belt holding the tocograph in position, since the record is not influenced by altering the tightness of the elastic belt. In fact, equally satisfactory measurements are secured if the belt is not employed.

The thickness of the abdominal wall plays little, if any, role in recording tonus. We have secured satisfactory records of tonus from a patient weighing 267 pounds. The magnitude of the uterine contents, likewise, do not appear to influence tonus appreciably. In the case of twin pregnancy, one patient may exhibit high, and another patient experience low tonus. In addition to these findings, variations occur in tonus in the same individual at different times.

The uterus of the present patient was extremely hard at all times and the degree of tonus registered by the tocograph appeared to be in proportion to this characteristic. From these observations, we conclude that the tocograph registers the intrinsic activity of the uterine wall.

## SUMMARY AND CONCLUSIONS

1. The uterine motility of a patient suffering from placental abruption was recorded throughout labor with a Lóránd tocograph.
2. The patient exhibited a persistently high uterine tonus, but at no time any significant intermittent uterine contractions.
3. The following subjects were discussed: (a) The influence of puncturing the membranes upon tonus, (b) the relation of the intermittent contractions to the effacement and dilatation of the cervix, and (c) the definition of the term "tonus."

### PREGNANCY AND LABOR IN A PATIENT WITH CARDIAC ANOMALY, PROBABLE TETRALOGY OF FALLOT

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CONGENITAL heart disease complicating pregnancy is a very uncommon condition. Hamilton and Thomson<sup>1</sup> reported 28 cases of recognized congenital heart disease among 48,190 women delivered at the Boston Lying-in Hospital, an incidence of 1 in 1,721 cases of pregnancy. Mendelson and Pardee<sup>2</sup> listed 20 cases of recognized congenital heart disease in approximately 31,000 obstetric patients at the New York Lying-in Hospital, a frequency of one in about 1,550 obstetric patients.

In the former series there are only 2 cases which fit into the cyanotic group of Maude Abbott; i.e., congenital cardiac defect with cyanosis due to permanent venous-arterial shunt. In the group of patients described by Mendelson and Pardee, there are 8 with pulmonary stenosis, and the authors could find only 25 others reported. In some of these there may have been other associated cardiac defects as well, and in a few instances the existence of the tetralogy of Fallot may be suspected (Case 6 of Mendelson and Pardee;<sup>2</sup> one case [p. 320] of Hamilton and Thomson<sup>1</sup>).

Because of the infrequency of reported cases of congenital cardiac disease complicating pregnancy and because of the paucity of reports of successful childbirth in patients with suspected tetralogy of Fallot, it was considered worth while to describe the following case, in which such a diagnosis was tenable.

## CASE REPORT

V. S. (History No. B-13295), a 20-year-old white female, was first seen in the outpatient department of the Sinai Hospital on Jan. 14, 1942. She was at that time seven and one-half months pregnant and had come to register as an obstetric patient.

*Family History.*—The patient was the sixth of seven children, the others being apparently normal. Her mother died of infection following her last pregnancy. The family history was otherwise essentially negative.

*Past History.*—The patient was born Dec. 15, 1921, following a normal pregnancy. She had had no scarlet fever, pneumonia, diphtheria, rheu-

matic fever, chorea, or pleurisy. She recalled no serious illnesses. Systemic history was essentially negative except as described under present illness.

*Present Illness.*—The patient stated that she “had always had heart trouble” for as long as she could recall. She had shortness of breath on climbing one flight of steps and on walking short distances on level ground. Her finger tips and lips would turn blue after climbing steps. She never had orthopnea or ankle edema. She noticed no increase in the severity of these symptoms with the passing years. She did take physical education in public school, although she experienced shortness of breath after exertion. She had never had any dizzy spells, syncope, or precordial pain.

She was married in April, 1941. Her last menstrual period began May 21, 1941. Previous menses had been normal. She continued to feel well and to do her housework. In July, 1941, she consulted her local doctor. She was told she was pregnant, with estimated date of confinement Feb. 27, 1942. Her heart was not examined at this time, and she was given no special instructions. She pursued her usual activities, and toward the beginning of January, 1942, she began to notice increasing dyspnea on exertion, with an occasional feeling of dizziness. Jan. 11, 1942, she began to notice swelling of her ankles, and also her finger tips and lips turned blue more readily after slight exertion.

*Physical Examination.*—(Jan. 14, 1942.) The patient was a well-developed, well-nourished, 20-year-old, white female. No edema was noted. There was pronounced clubbing of the fingers and suggestive clubbing of the toes. There was moderate to marked cyanosis of the fingers and lips. Respirations were rapid even at rest (26 per minute) with dyspnea on slight exertion. The face was flushed. There was no venous distention. Examination of the head and neck revealed nothing unusual. The patient's chest was well formed and symmetrical. The lungs were normal. Abdominal examination disclosed an intrauterine pregnancy of approximately thirty weeks' duration, with the fetus lying in the vertex position. Fetal heart sounds were heard over the left lower quadrant. The liver and spleen were not palpable.

*Heart:* No unusual precordial pulsations were visible. On percussion the upper left heart border seemed prominent, and the apex of the heart seemed to be displaced somewhat to the left. The right border of the heart could not be percussed beyond the right sternal margin. The point of maximum impulse was in the fifth left intercostal space just outside the mid-clavicular line. There was a coarse systolic thrill and systolic thrust over the third intercostal space next to the sternum, with a visible lift over this area. The heart rhythm was regular, and there were no extra systoles. The heart sounds were forceful and of good quality. At the apex there was heard a loud first sound, followed by a long, high-pitched systolic murmur of moderate intensity. One observer thought there was a slightly blurred accentuated third heart sound early in diastole at the apex. At the base of the heart there was a long, loud, harsh systolic murmur to the left of the sternum in the third intercostal space, rather well localized. The second heart sound over this area was loud, sharp, and ringing. To the right of the sternum over the base of the heart the sounds were not very intense and were essentially similar to those heard to the left of the sternum at this level, except that the second heart sound was not as accentuated. Blood pressure was 132/94. The radial pulses were normal.

*X-ray of Chest.*—(Fig. 1.) The right cardiac border measured 5 cm. and the left 8.6 cm. from the midline. The transverse diameter of the aorta was 4.5 cm. The transverse diameter of the thorax measured 25 cm. There was a fullness of the pulmonary conus, and the heart appeared slightly enlarged. The lung markings were accentuated on both sides with some calcified shadows noted in the hilar regions. (This was a six-foot plate.)

*Fluoroscopic Examination.*—*Posteroanterior view:* The pulmonary conus appeared prominent. The aortic knob seemed normal. There were some small pulsations in the right hilar regions. *Left anterior oblique view:* The right ventricle appeared larger than the left. The aorta seemed normal, and the pulmonary artery could not be visualized. *Right anterior oblique view:* The right ventricle appeared enlarged. The left auricle was normal, and the right auricle was not transected by barium in the esophagus.

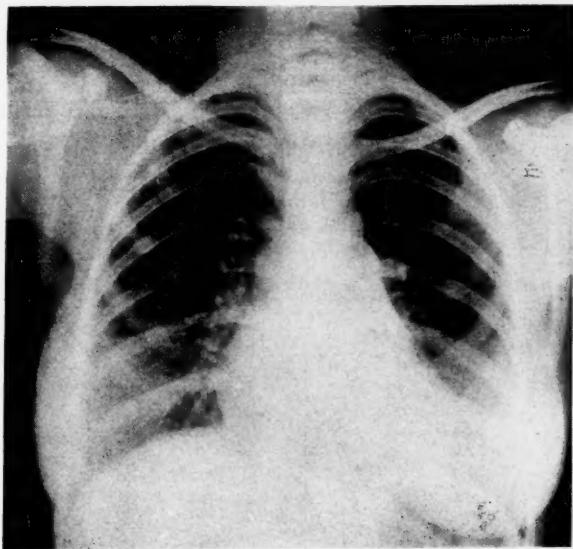


Fig. 1.—X-ray of chest. Note the prominence of the pulmonary conus. The heart appears slightly enlarged.

*Electrocardiogram.*—(Fig. 2.) Rate 107 per minute. P-R interval 0.18 seconds. QRS duration normal. Sinus tachycardia. Right axis deviation.  $T_1$ ,  $T_2$  and  $T_4$  upright.  $T_3$  inverted. ST-segments normal. No  $Q_4$ .

*Stethogram.*—(Fig. 3.) *Apex:* There was a loud first heart sound immediately preceded by a loud auricular sound occurring late in ventricular diastole. There was a long systolic murmur of moderate intensity ending in an accentuated second heart sound. There was no definite third heart sound. *Pulmonary area:* The first sound was followed by a long, loud, high-pitched systolic murmur. The second sound was accentuated and high pitched. There were no definite diastolic murmurs. *Aortic area:* The sounds were similar to those over the pulmonary area, but of louder intensity.

*Circulation Time.*—(Jan. 21, 1942.) Arm-to-lung (ether) time was 3.5 seconds. Arm-to-tongue (saccharin) time was 7.0 seconds. The



patient experienced tingling sensations in both hands and fingers after the ether was injected.

*Venous Pressure.*—(Jan. 21, 1942.) 6.75 mm. of water in left arm.

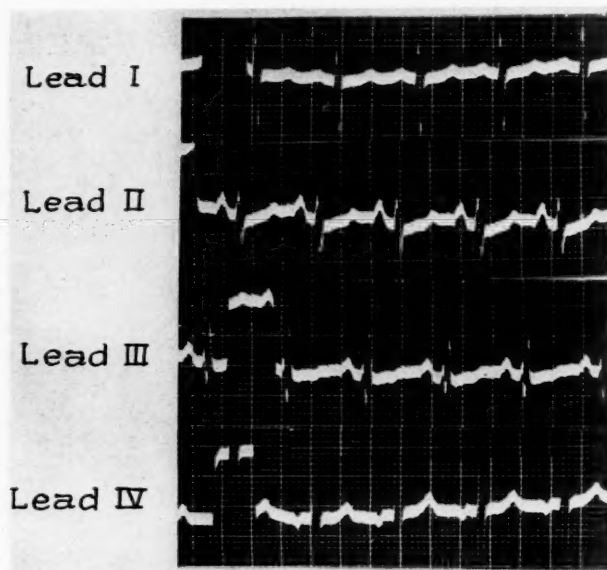


Fig. 2.—Electrocardiogram. Note the right axis deviation and the prominence of the P-waves.

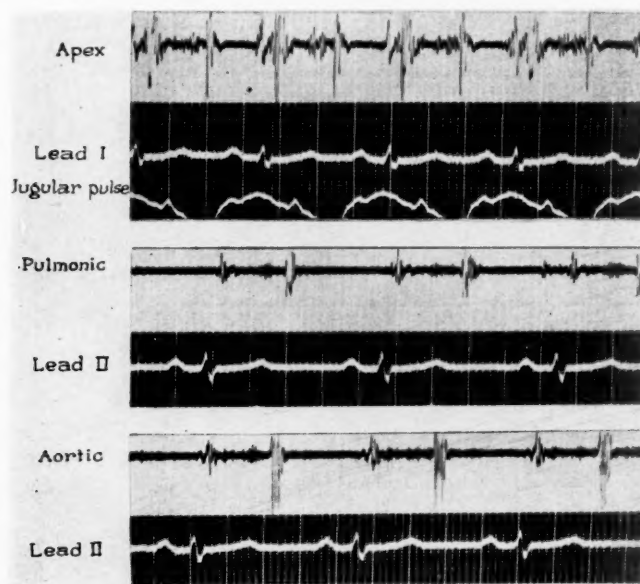


Fig. 3.—Stethogram. *Apex*: Loud auricular sound immediately preceding first heart sound, long systolic murmur, accentuated second heart sound. *Pulmonic*: Long systolic murmur following first heart sound, accentuated second sound. *Aortic*: Similar to pulmonic, but of greater intensity.

*Laboratory Findings.*—Serologic tests for syphilis were negative. Urinalysis was normal. Blood hemoglobin on Jan. 14, 1942, was 104 per cent of normal.

*Course in Hospital.*—The patient was admitted to the hospital immediately after being examined in the outpatient department. She was put to bed and digitalis was administered. On the day of admission she received 0.6 Gm. of powdered digitalis leaves. At 2:30 A.M. the following morning, January 15, the patient began to have labor pains. She was given a sedative. At 5:30 A.M., after a short labor, she was delivered by low forceps, following a pudendal block and episiotomy, of a live female child in the left occiput anterior position. The child responded immediately. The mother's blood loss was minimal, and repair of the episiotomy was easily accomplished. The child was later found to be entirely normal on physical examination. During the three-hour period of labor and delivery the patient had no unusual tachycardia or dyspnea. Her blood pressure dropped to 124/84 after delivery, and remained within normal limits thereafter. On January 16 the patient was subjected to a Pomeroy sterilization under local anesthesia, and easily withstood this procedure. Digitalization was completed after delivery, and the patient was then maintained on 0.1 Gm. of digitalis leaves per day. She left the hospital on Feb. 7, 1942. Examination six weeks later showed her to be in good general condition, with heart findings essentially unchanged. She was well compensated and was receiving 0.1 Gm. of digitalis leaves daily.

#### DISCUSSION

The clinical diagnosis of tetralogy of Fallot (dextroposition of the aorta, pulmonary stenosis, interventricular septal defect, and right ventricular hypertrophy) is admittedly a difficult one. In the case here described the pulmonary conus is full, rather than absent. The pulmonary stenosis is therefore probably valvular (at the pulmonary orifice) rather than prevalvular (stenosis of the pulmonary conus of the right ventricle). The sensation of tingling in the fingers, following the intravenous injection of the small amount of ether used in determining arm-to-lung circulation time, has been noted in patients with venous-arterial shunts, where some of the ether does not reach the lung; but is shunted to the left heart and reaches the peripheral circulation. Other factors supporting the impression of probable tetralogy of Fallot are the cyanosis and clubbing since birth, the right ventricular enlargement, the right axis deviation of the electrocardiogram, and the rough systolic murmur and coarse thrill at the base of the heart to the left of the sternum.

This case presents several interesting features in the management of obstetric patients with heart disease. The importance of a thorough physical examination of the patient as a routine when she is first seen by the obstetrician should be emphasized. In this case this was not done, and when she was examined at this clinic the patient was found to have organic heart disease and her pregnancy was well advanced, and she presented symptoms of cardiac embarrassment. While the final outcome was not unfavorable, this fortuitous result cannot always be anticipated. If, at the time of examination the patient's cardiac condition is found to be such that pregnancy should be interrupted, this can be accomplished more easily and with less danger to the patient early in

pregnancy. Thus early examination and diagnosis protect the patient and make possible more complete and better prenatal care.

The pregnant patient with organic heart disease should be examined more frequently than is the nonpregnant patient, for it is known that the burden upon the heart increases as pregnancy advances, reaching a maximum at about the eighth month. In pregnant patients with heart disease, as in similar nonpregnant patients, the indication for digitalis is heart failure. However, it should be noted that increasing dyspnea and tachycardia on exertion and orthopnea may be signs of beginning cardiac insufficiency, and that digitalis may therefore be indicated, especially as the load upon the heart may be expected to increase. If there is any question as to the cardiac condition being the basis for these symptoms, simple methods of determining a prolongation of the circulation and an increase in the venous pressure, more objective evidence of cardiac failure, are easily available. It is not necessary to wait for cyanosis, pulmonary and hepatic congestion and marked peripheral edema to appear before treating the patient for heart failure. Thus, this patient received digitalis not as a routine prophylactic measure, but as a therapeutic procedure.

Bed rest, daily afternoon naps, and restriction of physical activity may be used as prophylactic measures when indicated.

The authors wish to thank Drs. Charles R. Austrian and Helen B. Taussig for their help and suggestions, and Dr. M. W. Aaronson for permission to report this case from the Obstetrical Service.

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### ARTIFICIAL PYREXIA IN FOUR PREGNANT WOMEN

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CUSTOMARY teaching that maternal pyrexia or anoxemia exerts a deleterious effect on the fetus, in utero, has engendered a decided reluctance to induce fever during gestation. By and large sentiment has opposed the practice even when it is otherwise definitely indicated. The results of an inquiry among leaders in the field of physical therapy generally confirmed the truth of this statement although isolated reports of successful treatment of pregnant women were received. In only one instance, abortion, which occurred two weeks after treatment, was reported, but the duration of pregnancy was not stated. Since a dearth of factual information and a considerable controversy exist, a report concerning the results of treatment in four patients should be of value.

In each case, fever was induced by inductothermy with a Burdick fever cabinet. Following a light breakfast, the patient received an

TABLE I. ARTIFICIAL PYREXIA IN PREGNANCY, TREATMENT DETAILS

INTELLECT				TREAT- MENT BEGUN LUNAR MONTH	CONDITION FOR WHICH TREATED	FEVER THERAPY					LABOR		CHILD	
IDENTI- FICATION	HOSPITAL NO.	AGE	GRAVIDITY			DATE	TOTAL DURA- TION*	DURATION OF MAXIMUM	MAXIMUM TEMP.	PULSE	DATE	LENGTH AND TYPE	WEIGHT (GRAMS)	SEX AND CONDITION
No. 1 M. K.	38-20860	20	i	5	11/23/37 11/27/37 12/ 7/37	7.15 6.45 7.30	3.00 3.30 3.15	106.8 106.4 106.8	156 140 157	5/26/38	15 hr. 30 min. Spont.	3138	Female A. and W. at discharge	
No. 2 M. T.	39-730	23	i	6	4/15/39 4/18/39 4/21/39 4/28/39	6.00 2.45 5.15 5.45	3.00 1.25 3.45 3.30	105.0 104.9 104.6 105.5	156 160 162 160	8/11/39	3 hr. 50 min. Spont.	2730	Female A. and W. at discharge	
No. 3 B. S.	39-14692	16	i	9	11/11/39 11/13/39 11/21/39	3.30 3.45 2.45	3.45 2.00 0.15	103.6 103.5 102.0	160 148 136	12/20/39	73 hr. Low forceps	2730	Female A. and W. at discharge	
No. 4 P. R.	42-360	32	iv	7	1/22/42 1/24/42 1/27/42 1/30/42 2/ 2/42 2/ 5/42 2/ 7/42 2/10/42 2/13/42 2/16/42	3.45 3.45 4.15 4.15 5.30 4.45 4.15 4.45 6.00 5.45	2.00 2.00 2.15 2.00 2.15 2.00 1.15 2.00 2.30 2.15	104.8 105.6 104.8 104.8 105.6 105.8 105.4 105.4 105.4 105.2	144 154 152 148 142 152 144 140 144 152	4/18/42	1 hr. 6 min. Spont.	3765	Male A. and W. at discharge	

\*Hours and minutes.

intravenous injection of 800 c.c. of 5 per cent glucose in normal salt solution. Although sedatives were not routinely employed, paraldehyde was administered by mouth if the individual became restless. During the entire stay in the cabinet, oxygen was administered through a nasal catheter. Before return to the ward the intravenous injection of fluid was repeated.

Details of treatment and essential data regarding each patient are included in Table I. It can be seen that the first three patients were treated with considerable caution. Patient 1 (M. K.) was submitted to artificial fever for a total of 22 hours and 30 minutes, with exposure to maximum levels for only 9 hours and 45 minutes. Patient 2 (M. T.) and 3 (B. S.) received artificial fever for totals of  $19\frac{3}{4}$  hours and 10 hours, with exposure to maximum temperatures for  $11\frac{1}{4}$  hours and 6 hours, respectively.

Despite the normal outcome of these three pregnancies and considerable improvement in the basic arthritic condition for which fever was induced, no other patients were treated for two and one-half years. Unquestionably, fear that treatment would inevitably lead to disaster prevented too great enthusiasm. However, the taboparesis of Patient 4 (P. R.) was so far advanced upon admission it was felt nothing could be lost and much might be gained by energetic treatment. Consequently, she received 10 treatments with a total duration of artificial pyrexia of forty-seven hours, and exposure to temperatures above  $104.8^{\circ}$  F. for twenty and one-half hours. Her general condition improved remarkably and the pregnancy was apparently unaffected. Prior to treatment she could not be left unattended, whereas immediately after therapy as well as at her second admission for delivery, her general demeanor was essentially that of a normal woman.

#### DISCUSSION

It has long been recognized that febrile illness, and pneumonia in particular, are prone to produce intrauterine fetal death with subsequent abortion or premature labor. Although the mechanism of the causation of fetal death is unknown, fever and anoxia, among other things, have been indicated. It should be pointed out that febrile illnesses, even those with diurnal swings in the temperature curve, produce a more or less constant fever. This is not the case with artificial pyrexia since the febrile periods are necessarily of short duration. None of the present series of four patients was submitted to artificial fever for more than seven and one-half hours at a single session and in each instance was allowed a minimum recovery period of thirty-six hours before the next treatment.

It is conceivable also that artificial pyrexia may exert a deleterious effect on the embryo or early fetus, without harming one in the second



or third trimester. Since none of our patients received treatment prior to the fifth lunar month, comment on this point is not justified.

Therapeutic results, even as consistent as these, do not warrant sweeping claims or deductions. On the other hand, it cannot fail to be of general interest that four women in the second and third trimesters of pregnancy were treated by the artificial induction of fever without observable damage to the fetus, in its subsequent intrauterine or early postnatal existence.

### PORTES CESAREAN SECTION

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**B**ECAUSE of the few instances reported of this operation we add this case to the literature on the subject.

This 21-year-old white woman was admitted to the hospital Feb. 19, 1942, in her second pregnancy and about three weeks from term. Her first pregnancy had terminated spontaneously at seven months and the baby had died shortly after birth.

When first seen her temperature was 100.2° F. and pulse 140. Blood pressure 140/90. She was rather obese. Urine showed a trace of albumin and a few bacteria. The membranes had ruptured thirty-six hours previously and she had been in fairly good labor since. The fetus was lying transversely with the head on the right and the buttocks on the left. The left arm protruded from the vagina almost to the shoulder and was macerated. Her home physician had made unsuccessful attempts to deliver her.

An examination showed the cervix fully dilated and the left shoulder impacted in the pelvis. The uterus was contracted so tightly about the fetus it was impossible to deliver her through the vagina. The fetal heart could not be heard and she stated that she had not felt the baby move since the previous day.

Since the patient was a young woman with no children, was definitely infected, and was in poor condition for a Porro section, we decided to do a Portes operation.

Under general anesthesia the abdomen was opened and the uterus delivered. As the uterus was very wide in the lower part due to the transverse presentation there was nothing to be gained by suturing the peritoneum before the uterus was opened. Tapes were placed around the uterus, and it was opened in the midline. A stillborn fetus was removed and the placenta extracted. The uterus was closed with three layers of continuous sutures. The abdomen was then closed in layers around the uterus.

Wet packs were kept on the uterus and sulfathiazole was started by mouth. There was some abdominal distention during the first twenty-four hours but none thereafter. Temperature was 103.6° F. the following day and pulse still around 140. Temperature thereafter was 100°

to 101°, and pulse around 100. There was a small amount of purulent drainage along the line of sutures in the uterus but the incision healed well.

On March 1 papules about 1 cm. in diameter appeared on the extensor surfaces of the extremities, and the conjunctiva was injected. Sulfathiazole was discontinued and the rash disappeared. The temperature returned to normal in twenty-four hours and remained normal.

On March 17, twenty-six days after the first operation, under general anesthesia, the attachment of the uterus to the abdominal wall was separated and the old incision opened for a distance about two inches above the uterus. The fat in this area was dark in color and showed evidence of old infection. The uterus was dropped back into the abdominal cavity and the abdomen closed, with a drain in the abdominal wall in the area of the old infection. Sulfathiazole was started again. Temperature rose to 101° the following day and 103° on the third day. Skin lesions reappeared at the same site as before so sulfathiazole was discontinued. The temperature immediately fell to normal and remained there throughout her stay in the hospital. Apparently she was very sensitive to sulfathiazole and this caused the rise in temperature.

The wound broke down for a distance of about two inches, corresponding to the area that was above the uterus. The fascia healed well. Since she had one and one-half to two inches of fat in the abdominal wall, it took it some time to granulate and the remainder of her stay in the hospital was necessary because of this. She was discharged April 25, sixty-five days after admission and thirty-nine days after the second operation.

#### COMMENT

This operation should be reserved for those cases of frank infection where the patient is a poor risk for section or where the patient is in her early reproductive life and very anxious to have a child. Since the introduction of the sulfa drugs, it should be considerably safer than formerly. Wound infection is the most frequent complication, and, as illustrated in this case, prolongs the hospital stay.

200 WEST SECOND STREET

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#### ALLERGIC SHOCK CAUSED BY SYNAPOIDIN\*

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**S**YNAPOIDIN is a combination of gonadotropin from human pregnancy urine and extract of anterior pituitary. It is biologically standardized by the method outlined by Mazer and Ravetz<sup>1</sup> in their preliminary report. Emphatic warning is given on the package that this medicament must be used with caution and under close medical observation, since it may cause severe reactions in the form of "enlargement of the ovaries, lower abdominal pain, and tenderness." No mention is made of its possible allergenic quality and examination of the available literature shows no report of shock from its use. Since, according to current medical opinion, the preparation is effective in the treatment of amenorrhea and of dysfunctional uterine bleeding, and its use is be-

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\*A product of Parke, Davis & Company.

coming more general, the publication of this report is thought to be desirable.

CASE 1.—A white woman, married, nullipara, aged 40, has for years been subject to perennial allergic rhinitis with seasonal (but not premenstrual) exacerbations. She is not sensitive, either clinically or by skin test, to meat proteins or animal emanations. Her inhalant symptoms are readily controlled by appropriate intradermal therapy with extracts of mold spores and local pollens. On the occasion of one such treatment she remarked that she wished there were "some sort of shot" that would as easily relieve her of another annoyance. Inquiry elicited the following history:

Her menses, which previously had been fairly normal, had in her thirty-first year become excessive, with interval bleeding so severe that anemia developed. Antuitrin-S was used with no result; pituitrin increased both the cramps and the metrorrhagia; theelin had a similar effect. Finally, one application of radium was used. After this, her dysfunctional bleeding ceased, her general health improved, and the menses were normal for several years. When she was 38, the menorrhagia and metrorrhagia recurred briefly, subsiding without treatment; the present recurrence, with almost continuous bleeding, seemed to be growing worse. She had no symptoms of the climacteric.

Synapoidin, 1 c.c. (15 units), was administered intramuscularly on April 25, 28, and May 2, 1942. There was no constitutional reaction. Metrorrhagia decreased after the first dose and ceased after the second. Menstruation, normal in other respects, appeared six days early. It was considered advisable to repeat the course. The patient reported on May 12, received 1 c.c. of synapoidin intramuscularly, and left the office. Our invariable technique of retraction on the plunger, initially and at intervals during the slow injection, was followed. No blood appeared in the syringe, and to the extent that this technique is reliable it is certain that the needle point was not in a vein.

About eighteen minutes later the patient returned, said that she was feeling rather odd, and collapsed. The diagnosis was obvious. A scarlatiniform discoloration was present on her chin and cheeks, dyspnea was marked, and she was in great distress. In spite of an immediate injection of adrenalin, promptly repeated, her anaphylaxis progressed rapidly. The scarlatiniform discoloration spread quickly to the trunk and arms; massive urticaria appeared about the eyes; the extremities quickly became swollen. Waves of nausea were followed by intense abdominal pain, only partially relieved by morphine and atropine. Presently the punctate erythema was replaced by blotches of urticaria, which faded and reappeared as the continuing adrenalin dosage prevailed or failed of control. No rigors had occurred, but later there was profuse sweating. The oral temperature, observed then for the first time, was 100° F.

The patient was kept under observation for six hours, her symptoms gradually subsiding. Nausea, abdominal discomfort, and occasional episodes of urticaria persisted until the following morning.

Four days later she was tested intradermally with a 1:5 dilution of synapoidin. A strongly positive atopic reaction, with typical wheal, flare, and intense itching, appeared in five minutes and persisted for several hours. This same dilution of synapoidin was then used as an intradermal test on a considerable number of children and adults of both sexes. Nearly all of them were known to be allergic. It produced

no reaction, or a slight and transient irritative response; or, in certain women, a brief blanching of the skin at the site of injection. Evidently no significant quantity of histamine is present in synapoidin. Passive transfer to recipients who showed no reaction to direct testing resulted in immediate and typical positive skin tests in the injected sites, at intervals of from one to five days after receiving the donor's serum.

#### COMMENT

Certain features of this case are of interest, not only to the clinician who may employ synapoidin in treatment, but to students of endocrinology and of allergic disease. This patient became hypersensitive to synapoidin after a therapeutic exposure lasting only seventeen days. Ten days intervened between the third uneventful injection and the fourth, which produced shock. Clinical and dermal sensitivity must have appeared at some time during that ten-day period, in which also the catamenia took place. And this sensitivity was specific to some constituent of the gonadotropic preparation; ample proof of such specificity has been offered. The active constituents are chorionic gonadotropin and pituitary extract, synergistically combined. These are similar to or identical with the secretions of the patient's own endocrine glands. Further, one or both of these hormones must have been relatively deficient, because the synapoidin corrected her dysfunctional bleeding.

Specific sensitivity does not develop overnight in human beings. Repeated adequate exposure is required. Is it possible that this allergic individual had built up a defense against her own hormones, causing their deficiency, and that the three intramuscular doses exhausted her antibodies?

From the clinical angle the matter is less complex. About 10 per cent of American women are actually or potentially allergic. Of these, a certain number will present indications for synapoidin therapy, and undoubtedly some of them will get it. Therefore, it is suggested that caution be exercised in administering this potent biologic preparation to women who have a personal or family history of allergic disease; that the dosage be kept low; and that the diluted material, say 0.02 c.c. of a 1:5 dilution, be used as an intradermal test when, because of the catamenia or for any other reason, a week or more has passed since the preceding dose.

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1105 PROFESSIONAL BUILDING



## A RARE CONNECTIVE TISSUE TUMOR (MYXOSARCOMA) IN THE AREA OF THE BARTHOLIN GLAND

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CONNECTIVE tissue tumors in the area of the vulvovaginal gland are rare and may originate either from vulvar elements or from the terminations of the round ligament. Only two cases of sarcoma of the vulvovaginal (Bartholin) gland have been reported in the literature.<sup>1, 2</sup> Because of the rarity, we wish to report the following case:

Mrs. G. W. (Hospital No. 110,616), aged 44 years, was admitted to the Bronx Hospital service of Dr. Smiley, on April 30, 1940. Aside from a slight thyroid disturbance some seven years earlier which had responded to medical treatment, her past history was essentially negative. She was a gravida iv, para ii, having had one spontaneous miscarriage, one induced abortion, and two normal spontaneous deliveries. Her menstrual history was fairly normal, beginning at the age of 12, with a twenty-seven- to twenty-eight-day cycle, and a flow lasting about five days. Her last regular period was on April 14, 1940, about two weeks before admission to the hospital.

With the ending of this period she began to complain of a burning sensation in the region of the right labia minora, followed soon thereafter by her noticing the presence of a mass. Within the next ten days this mass progressively increased in size. There was no pain.

Physical examination was relatively negative, except for the presence of the tumor situated in the right labium, about the size of a hen's egg, and extending into the right vaginal wall. It felt to be semisolid in character, quite tense but not fluctuant.

Under general anesthesia, the entire mass was easily enucleated on May 1, 1940. She was discharged on May 7, 1940, after an uneventful recovery.

Examination of the specimen (Path. No. 18178) showed a 4 cm. round, pinkish white, well-encapsulated soft mass of tissue which, on section, was soft, yellowish white and homogeneous. Microscopic sections revealed a rather homogeneous, loosely textured connective tissue, containing a number of lymphatic vessels and some small blood vessels. A few mucous glands were present. Diagnosis: Fibroma (Fig. 1).

She was readmitted to the hospital on Dec. 22, 1941 (Hospital No. 129097), with the following history: For the past three weeks there had been considerable pain at the site of the previous operation, for which local applications had been applied with no relief. Several attempts had been made to dilate the duct of Bartholin's gland, without success. Soon thereafter, a small mass appeared which had increased rapidly in size.

Examination at this time revealed the presence of a large, firm non-fluctuant tumor mass, about the size of an orange, which extended upward and bulged into the vagina, occupying more than one-half of the



right side of the vagina. The skin and mucous membrane covering the tumor were purplish red in color, very tense and very painful on palpation.

Under cyclopropane anesthesia, an incision was made over the mass and a large amount of a grayish semisolid gelatinous material was removed. No abscess cavity was seen, nor was there any fluid present. The entire cavity was carefully examined and thoroughly evacuated.

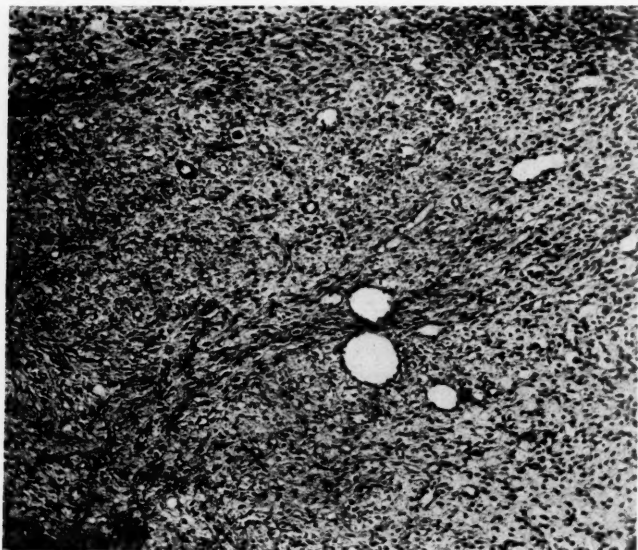


Fig. 1.—No. 18178. Homogeneous, loosely texture connective tissue containing a number of lymphatic vessels and some small blood vessels. Diagnosis: Fibroma.

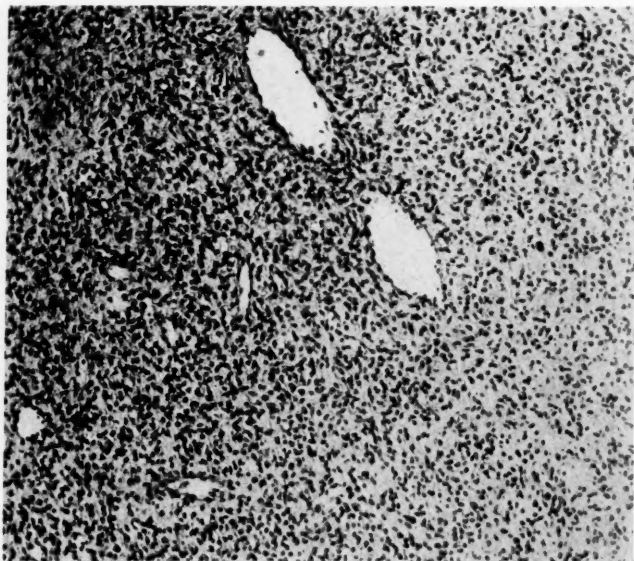


Fig. 2.—No. 21886. Very cellular spindle cell tumor with some areas of myxomatous-like structure and slight tendency to hyperchromatism. Diagnosis: Myxosarcoma.

Interrupted chromic catgut sutures were used, to close the entire cavity, and the patient was returned to bed in good condition.

The specimen submitted for pathologic examination (Path. No. 21886) consisted of several irregular portions of grayish yellow gelatinous material. Microscopic sections revealed a very cellular spindle cell tumor with some areas of distinct myxomatous-like structure. There was a slight tendency toward hyperchromatism. *Diagnosis:* Myxosarcoma (Fig. 2).

*Follow-up:* Several courses of deep x-ray therapy were given over the operative site. In February, 1942, she began to complain of backache, radiating to the right side. A complete x-ray study was made of her lungs, as well as of the skeletal structures, all of which were negative. She was last seen in April, 1942, at which time there were no complaints. The operative site was free from any pathology.

#### DISCUSSION

The Bartholin gland is surrounded by the perineal fascia and by a coat of striated musculature of which some fasciculi penetrate into the interior of the gland and are located in the connective tissue septa between the lobes of the gland, together with smooth muscle and elastic fibers. Although a genetic relationship between the tumor and the connective tissue which participates in the structure of the gland could not be proved histologically, we feel justified to assume this possibility on the basis of the localization of the tumor and in the absence of proof to the contrary. Clinically, the gradually growing tumor furnished the typical picture of a retention cyst of the gland of Bartholin.

We are indebted to Dr. Joseph Felsen, Director of Laboratories and Medical Research, for the photomicrographs.

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900 GRAND CONCOURSE  
1840 GRAND CONCOURSE

## ANTE-PARTUM RUPTURE OF THE UMBILICAL VEIN

### REPORT OF ONE CASE

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**I**NTRAUTERINE intra-partum rupture of the umbilical cord has been reported by Bloxsome,<sup>1</sup> Vermelin,<sup>2</sup> Zocchi,<sup>3</sup> Siddall,<sup>4</sup> and Sackett.<sup>5</sup> Complete rupture of the umbilical cord during labor is of more frequent occurrence than is partial rupture which may involve the vein and one or both arteries and result in hematoma formation.

Intrauterine ante-partum rupture of the umbilical vein producing a hematoma of the cord with resulting fetal death has not been reported. This case is presented in illustration of this condition.

The patient was a 25-year-old primigravida. The entire prenatal course was uneventful, and the blood pressure and weight gain were within normal limits.

Two weeks before the estimated date of confinement abdominal and rectal examinations were made. The uterus was enlarged to the size of a term pregnancy, the lie longitudinal, and the presentation cephalic. The fetal heart tones were heard in the lower left abdominal quadrant at the rate of 130 per minute. Three days later the patient reported the absence of fetal motion. Examination at this time showed the lie and presentation to be the same as on the previous examination. The cervix was partially effaced, 2 cm. dilated, and the presenting part was at the level of the ischial spines. Fetal heart tones were not heard and fetal motion was absent.

Labor began spontaneously the following day and the patient entered the hospital. Labor was conducted under sodium amytal and scopolamine analgesia.

Delivery of a stillborn male child was accomplished by prophylactic forceps extraction preceded by a right mediolateral episiotomy under nitrous-oxide-ether anesthesia.

The duration of labor was twelve hours and thirty-five minutes. The first stage was eleven hours, the second stage one hour and 20 minutes, and the third stage fifteen minutes.

At delivery it was noticed that the umbilical cord for a distance of about five inches from the umbilicus was greatly swollen and discolored. The entire cord measured 55 cm. in length, and the placental insertion was central. The stillborn baby, with the exception of slight maceration, appeared normal in form. The cord and placenta were sent to the laboratory for examination with permission for an autopsy upon the baby.

*Laboratory Report.*—The body was that of a well developed male measuring 52 cm. in length. There was some post-mortem liquefaction and degeneration. The placenta and umbilical cord represented the chief pathology. The placenta measured 14 by 13 by 3 cm., and the maternal surface showed the cotyledons to be intact and upon cut sec-

tion grossly normal. The fetal surface of the placenta was also normal, with the cord taking an approximately central origin. At the fetal end of the cord and continuous with the umbilicus was a large aneurysmal-like thickening and widening of the cord extending over an area measuring 14 cm. in length. In this dilated portion the cord measured  $2\frac{1}{2}$  cm. in one diameter and  $1\frac{1}{2}$  cm. in the other. It was darkly discolored and apparently hemorrhagic in character. Upon cut section the two arteries were found to be of normal size and the walls of the usual thickness. These arteries showed no pathologic changes. About the arteries and completely infiltrating and replacing the myxomatous substance of the cord was an extensive hemorrhage which was dark in color and firm and friable in consistency. The region of the umbilical vein was completely destroyed and replaced by a cavernous type of hemorrhagic sinus which represented a complete rupture of the umbilical vein. Beyond this and toward the placenta, the umbilical vein and arteries were markedly engorged and somewhat dilated. The peritoneal surface of the umbilicus showed no pathological changes. The continuation of the umbilical structures into the urachus and the continuation of the umbilical vessels to the liver showed no anatomic changes and no pathologic conditions.

*Diagnosis.*—(1) Intrauterine rupture of the umbilical vein just proximal to the umbilicus. (2) Massive hematoma of the umbilical vein. (3) Post-mortem liquefaction and degeneration of an otherwise normal fetus. (4) Apparent death in utero.

#### COMMENT

The suggested causes of rupture of the umbilical cord or its component parts are varied. A short cord and syphilis are mentioned most frequently but the accidents reported in which these causes were present occurred during labor. Anomalies of the cord vessels have been suggested as predisposing factors, especially weakness of the vessel walls which rupture especially when the blood is squeezed out of the placenta during a labor contraction.<sup>6</sup> None of the mentioned causes were a factor in this case.

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# Department of Practical Problems in Obstetrics and Gynecology

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CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

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## TREATMENT OF HEART DISEASE IN PREGNANCY

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**H**EART disease is one of the most serious complications of pregnancy and responsible for about 10 per cent of all maternal deaths. This, if anything, is a conservative estimate, as indicated by most of the statistics from the maternity hospitals in this country. In our obstetric service, organic heart disease accounts for over 10 per cent of the total maternal mortality.

This paper is based on a study of 676 patients with organic heart disease admitted to the Lying-in Hospital (Woman's Clinic of The New York Hospital) during the period Sept. 1, 1932, to Dec. 31, 1940, although in certain of the data, the statistics for 1941 are included. During the period ending last December, we had 7 maternal deaths from cardiac disease in 34,353 consecutive pregnancies, giving a death rate of 10.3 per 1,000 pregnancies, or a rate five times greater than that for the clinic (1.98 per 1,000).

The incidence of organic heart disease in our obstetric patients was 2.78 per cent during the eight years ending 1940; 676 cardiac patients in 24,289 deliveries.

In the study and management of these patients we have employed the functional classification of the New York Heart Association, which may be described briefly as follows:

- Class I. No limitation of physical activity.
- Class II. Slight limitation of activity.
- Class III. Marked limitation of activity.
- Class IV. Complete limitation of physical activity (bed rest).

Undue fatigue, palpitation, dyspnea and anginal pain are the symptoms of cardiac involvement should the patient exceed the limitation of activity described for each group in this classification. In order to



TABLE I. CAUSES OF MATERNAL MORTALITY FOR THE PERIOD SEPT. 1, 1932, TO DEC. 31, 1941

67 Cases in 34,353 Consecutive Pregnancies  
Pavilion, Private, and Outdoor Services

	NUMBER OF CASES	PERCENTAGE
Infection (ante-partum, post-partum, postabortal)	13	19.4
Pulmonary complications	10	14.8
Post-partum hemorrhage	9	13.4
Cardiac disease	7	10.4
Pneumonia	6	8.9
Toxemia of pregnancy	4	6.0
Premature separation of placenta	3	4.5
Cerebrovascular accident	3	4.5
Pyelonephritis	2	3.0
Circulatory collapse	2	3.0
Postoperative hemorrhage	1	1.5
Tuberculosis, miliary	1	1.5
Placenta previa, ante-partum	1	1.5
Chorionepithelioma	1	1.5
Blood dyscrasia, erythroblastic-splénomegaly	1	1.5
Psychosis, reactive panic (suicide)	1	1.5
Peritonitis, after appendicitis	1	1.5
Not determined, insufficient data	1	1.5
Total	67	99.9
Total maternal mortality rate		1.98 per 1,000 pregnancies

TABLE II. INCIDENCE OF HEART DISEASE IN PREGNANCY SEPT. 1, 1932, TO DEC. 31, 1940

Total pregnancies, including abortions	24,289
Patients with classified heart disease	676 or 2.78 per cent

determine the amount of physical activity which should be permitted in each case, we have utilized, during the past two years, the following "therapeutic classification," in association with the functioning groupings of the New York Heart Association:

- Class A: Patients with cardiac disease whose physical activity need not be restricted.
- Class B: Patients with cardiac disease whose ordinary physical activity need not be restricted, but who should be advised against unusually severe or competitive efforts.
- Class C: Patients with cardiac disease whose ordinary physical activity should be moderately restricted, and whose more strenuous habitual efforts should be discontinued.
- Class D: Patients with cardiac disease whose ordinary physical activity should be markedly restricted.
- Class E: Patients with cardiac disease who should be at complete rest, confined to bed or chair.

In general, the therapeutic classification follows closely the functional grading of the cardiac capacity, so that the patient in Class I would be given an "A" or "B," in other words, Class IA or IB. There are, how-

ever, marked exceptions, where, for example, rheumatic activity exists. In such an instance the grouping may be Class IE.

TABLE III. DISTRIBUTION OF PATIENTS WITH HEART DISEASE ACCORDING TO THE FUNCTIONAL CLASSIFICATION OF THE NEW YORK HEART ASSOCIATION

	PATIENTS	PER CENT
Class I	300	44.3
Class II	297	43.9
Class III	60	8.9
Class IV	19	2.8
Total	676	99.9

Most of our patients, 88 per cent, were placed in Class I and Class II, as indicated in Table III. These constitute the milder cases of heart disease and ordinarily are not accompanied by a greatly increased maternal mortality. It is the patients in Classes III and IV that cause the greatest concern, not only from the standpoint of mortality, but also with regard to the advisability of continuation of the pregnancy and the method of delivery. It must be pointed out, however, that a patient in Class II, and even one in Class I, may become a serious problem as gestation proceeds, or during and following labor.

From this emphasis placed upon the functional interpretation of heart disease, it must not be concluded that we neglect diagnosis and evaluation of the cardiac lesions. On the contrary, at the first examination of a suspected cardiac patient, a competent cardiologist checks the findings as they relate to the heart. In order to obtain a correct diagnosis as early as possible during gestation and to provide adequate medical prenatal care, we conduct a special-cardiac clinic, weekly, under the joint supervision of internists and obstetricians.

Mitral stenosis, either alone or with insufficiency, is usually the most frequent lesion. Rheumatic heart disease accounts for almost 95 per cent of our cardiac patients, while congenital heart disease constitutes about 2 per cent of all organic heart disease. Uncomplicated aortic regurgitation is seen in approximately 3 per cent of the cardiac patients.

The group of women with congenital heart disease complicating pregnancy is relatively small, due no doubt to the fact that the majority of patients with serious congenital cardiac lesions die before the age of puberty. The physician is sometimes consulted regarding the advisability of marriage and pregnancy in patients with congenital heart disease. There can be no doubt that an intelligent answer to this question rests upon a careful evaluation, involving cardiac functional capacity determination, measurement of the size of the heart, consideration of the specific cardiac lesion and estimation of the degree of cyanosis and polycythemia. Mendelson and Pardee conclude that cyanosis *per se* is not a contraindication to pregnancy. In coarctation of the aorta they advise contraception because of definite and increased risk associated

with pregnancy in this condition. Should the patient be pregnant, therapeutic abortion is indicated unless the pregnancy is too far advanced, in which event cesarean section and tubal sterilization should be considered.

As rheumatic heart disease accounts for over 90 per cent of our cases, observations regarding the average age at death of patients with this disease are of great significance, particularly as regards prognosis. In a study of 1,633 patients with rheumatic heart disease, De Graff and Ling found the average age at death to be 33 years. Reid, likewise, reports an average age at death of 35.5 years and further notes that for married women with heart disease the average age at death is about five years less than for unmarried women with this disease.

When pregnancy occurs in a cardiac patient, the first and perhaps most important question to be faced is whether she will be able to go through pregnancy, labor, and the puerperium with a fair degree of safety. From an evaluation of her cardiac status, or, in other words, an estimation of the extent of cardiac damage, we are able to make a fairly accurate prognosis in the majority of cases. However, there are other factors, such as infection, which may come into play as pregnancy advances, and over which we have little or no control. In every gravid woman with cardiac disease one is faced with the question: What are the chances of this patient developing cardiac failure in pregnancy, labor, or the puerperium? A correct answer must be sought most earnestly because the maternal mortality rate in women developing congestive heart failure is many-fold that occurring in cardiac patients who do not become decompensated, either during or shortly after gestation.

The development of congestive heart failure will depend upon the degree of cardiac damage and upon certain extracardiac factors, such as upper respiratory infection and anemia.

Oppel, in a complete survey of all our patients with congestive heart failure, observed that decompensation developed in each of the last eight months of gestation as well as during the first day of the puerperium. He noted that the most frequent and important sign of heart failure during gestation is congestion of the lungs; furthermore, that age is a most valuable guide to prognosis. In 26 patients who developed congestive heart failure during pregnancy, or in labor, or in the early puerperium, Oppel found that in one-half of these cases the extent of cardiac damage was responsible for the failure in compensation, while in the other half extracardiac factors, such as upper respiratory infection, were the precipitating causes for the break. When cardiac failure did occur, its outstanding manifestation was congestion of the lungs, associated at times with hemoptysis and often progressing to pulmonary edema. The incidence of congestive heart failure in his 620 patients was only 4 per cent, a figure considerably lower than those previously reported. Oppel ascribed this low incidence to two factors, the selection of patients showing physical signs of passive congestion and the close antenatal supervision in a special cardiac clinic. He is convinced that heart failure was often prevented by careful management.

Carr and Hamilton report that the incidence of cardiac failure increases steadily from the third to the ninth lunar month of gestation, decreasing during the last month. In our cases, on the other hand, there does not seem to be any particular month of pregnancy when failure is most likely to appear. Congestive heart failure, as stated above, developed in each of the last eight months of pregnancy. Jensen, in a review of a large series of cases, likewise comes to the conclusion that there is no special period of pregnancy when decompensation is most likely to develop.

#### MANAGEMENT OF CARDIAC PATIENTS

As stated above, all cardiac patients are closely observed during the ante-partum period, in a special cardiac clinic. Every obstetric patient having a history of rheumatic fever, chorea, or previous heart disease is referred to this clinic for evaluation even though she may have no symptoms or signs at the moment. Patients with cardiac murmurs, dyspnea, unexplained ankle edema, or tachycardia are referred to this clinic. Each patient is carefully evaluated, laboratory tests, including determination of the vital capacity, electrocardiograms, and roentgenograms at a distance of 7 feet, being performed as indicated. The hemoglobin and cell volume are determined routinely, and the pulse and respiratory rate recorded.

Activity is restricted as indicated. This is especially necessary in the last trimester, although it may be indicated throughout pregnancy. At times, social service assistance with a housekeeper is employed. At times, especially since many of our patients lived on the top floor of apartment buildings (without elevators), it became necessary to urge moving to a ground floor apartment.

Patients seen in the first trimester of pregnancy with serious heart lesions are immediately admitted to the hospital for consideration of interruption of the pregnancy. Upper respiratory infections are regarded ominously, and the patient is frequently admitted for this indication, since experience teaches that this complication may precipitate a break in compensation. As term is approached, certain patients are admitted for rest and evaluation before delivery. This is especially valuable with regard to the mode of delivery.

Digitalis is not employed routinely. It is given on indication. Digitalization is accomplished usually in twenty-four hours. Ordinarily, this drug is given when required, and is not employed prophylactically. Pulse and respirations are charted during labor, and are of particular prognostic significance during the first stage of labor, as will be shown later.

Delivery was effected with the use of basal analgesia and local infiltration in a large number of patients having either spontaneous or operative delivery. This technique is a modification of that used by Urnes and Timmerman and has been described by me, as well as by my associates, Griffin and Benson. Local infiltration anesthesia is also frequently used

in cases of cesarean section where a general anesthetic is contraindicated. If the latter is employed in a patient with organic heart disease, it should be, in our opinion, open drop ether or ethylene.

In our clinic, Pardee and Mendelson studied the pulse and respiratory variations in 180 normal women in labor. They found that during the first stage of labor there was little change in the pulse and respiration rates. With the onset of voluntary muscular efforts, occurring usually at or shortly before full dilatation of the cervix, these rates may or may not increase. In 10 per cent of their cases, the pulse rose to over 110 per minute after the onset of voluntary efforts, while in 19 per cent the respiratory rate exceeded 24 per minute. It is noteworthy that they were unable to correlate the pulse or respiration levels with the use of analgesia or with any particular analgesic.

TABLE IV. TYPE OF DELIVERY IN HEART DISEASE COMPLICATING PREGNANCY

TYPE OF DELIVERY	CLASSIFICATION							
	I		II		III		IV	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Spontaneous delivery	224	74.6	178	59.9	19	31.6	3	15.7
Operative (cardiac indication)	12	4.0	53	17.8	21	35.0	10	52.6
Operative other	50	16.6	30	10.1	1	1.6	0	0.0
Abortions (therapeutic and spontaneous)	14	4.6	36	12.1	19	31.6	6	31.6
Total	300	99.8	297	99.9	60	99.8	19	99.9

In general, the mode of delivery varied with the classification of the heart disease. For example, spontaneous delivery was permitted in about 75 per cent of the patients in Class I, whereas, only 16 per cent in Class IV delivered spontaneously. When operative delivery (for cardiac indication) is analyzed, one finds that only 4 per cent of the patients in Class I had an operative delivery, whereas, in Class IV, nearly 53 per cent had this type of delivery. The percentages for Classes II and III are found midway between Classes I and IV.

Cesarean section was performed in 3.26 per cent of the patients with heart disease as shown in Table V. Again the incidence varies with the severity of the heart lesion. For example, no sections were performed in Class I, whereas, Class III and Class IV had an incidence of 32 and 50 per cent; respectively.

Therapeutic abortion was performed in 37 patients, or 5.4 per cent, the average incidence for the clinic being only 0.79 per cent. The incidence of interrupted pregnancies varies also with the Class of heart disease from which the patient suffered as shown in Table VI. The incidence was highest in Classes III and IV, which is to be expected, and ranged from 31 to 46 per cent.

Spontaneous abortion occurred in 5.1 per cent of the patients, which is less than the clinic incidence of 6.8 per cent for spontaneous abortion. The infantile mortality was not increased in this group and was 3.84 per



TABLE V. THE INCIDENCE OF CESAREAN SECTION IN PATIENTS WITH HEART DISEASE

	CLASSIFICATION			
	I	II	III	IV
Cesarean section (cardiac indication)	0	2	5	2
Cesarean section (and sterilization)	0	2	6	5
Total	0	4 (18.1 per cent)	11 (50 per cent)	7 (31.8 per cent)
Total incidence of cesarean section for heart disease			3.26 per cent	
Total clinic incidence of cesarean section			2.2 per cent	

TABLE VI. INCIDENCE OF THERAPEUTIC ABORTION IN HEART DISEASE

	NUMBER OF CASES	THERAPEUTIC ABORTION	
		NUMBER	PER CENT
Class I	300	0	0.0
Class II	297	18	6.0
Class III	60	13	46.1
Class IV	19	6	31.6
Total		37 cases	
Total incidence of therapeutic abortion for heart disease		5.4 per cent	
Total clinic incidence of therapeutic abortion		0.79 per cent	

cent. Therefore, the actual loss of fetal life because of heart disease occurred only in the group having therapeutic abortion, namely 5.4 per cent.

Prevention of conception was accomplished by tubal sterilization in a small number of patients, most of whom are in Classes III or IV. This procedure was performed at the time of section, as shown in Table V, or was effected on the third post-partum day under local anesthesia. The Madlener type of operation, or actual tubal resection, seems to give satisfactory results. Other patients in Classes II and III especially are referred to the contraceptive clinic for the necessary advice. Such is our practice, particularly if the patient has had only one child.

Mendelson and Pardee, in a recent study of the pulse and respiratory variations during labor in patients with rheumatic heart disease, found that in all their cases of intrapartum or post-partum heart failure, the pulse rate was elevated to 110 or over, either alone or with an increased respiratory rate of above 24 per minute during the first stage of labor. Furthermore, they observed no serious heart failure, irrespective of the functional classification, provided the pulse and respiration rates remained below these critical levels throughout the first stage of labor.

#### SUMMARY AND CONCLUSIONS

1. Organic heart disease is a most serious complication of pregnancy, being present in about 2 to 3 per cent of all obstetric patients and accounting for an increased maternal mortality (10.3 per 1,000), which is five times greater than that for our total obstetric patients (1.98 per 1,000).

2. Rheumatic heart disease accounts for almost 95 per cent of our cardiac patients.

3. Congenital heart disease, although rare, requires careful evaluation before pregnancy is contemplated. Of these cases, those with coarctation of the aorta should be dissuaded from childbearing and, if pregnant, should have the gestation interrupted if in the first trimester; on the other hand, should the gestation be beyond the first trimester, the patient may be carried to viability or term, with delivery by cesarean section followed by tubal sterilization.

4. Congestive heart failure occurred in about 4 per cent of our cardiac patients, and was associated with a maternal mortality of 15 per cent.

5. The development of decompensation depends upon such extra-cardiac factors as upper respiratory infection and anemia, as well as on the degree of cardiac damage. Cardiac damage per se is responsible for about one-half the cases of congestive heart failure, while extracardiac causes account for the remainder of the cases of decompensation.

6. Proper treatment and management require:

a. Early diagnosis and proper functional evaluation. This should be done in cooperation with an internist or cardiologist.

b. Very close and frequent supervision in a special cardiac clinic or in the doctor's office.

c. The interruption of pregnancy during the first trimester in those patients with organic heart disease, in whom congestive heart failure is liable to occur should gestation proceed to term. Therapeutic abortion, on the indication of heart disease, was performed in our clinic in only Classes II to IV and amounted to about 5.4 per cent of our cardiac patients.

d. In general, no interruption of pregnancy after the fourth month.

e. Rest and varying periods of hospitalization, as indicated, prior to delivery. In general, the period or periods of hospitalization will vary with the severity of the cardiac disease or the functional classification, ranging from several days in Class I to several months in Class IV.

f. Careful consideration of the method of delivery in each instance.

g. Close scrutiny of the pulse and respiration rates during the first stage of labor. A pulse rate of over 110 per minute and a respiratory rate of over 24 per minute must be regarded as danger signals.

7. Our patients who developed cardiac failure during or shortly after labor, showed a pulse rate of over 110, alone or associated with a respiratory rate of over 24 per minute, in the *first stage* of labor. In these cases, rapid digitalization, with forceps delivery upon full dilatation of the cervix, is the treatment of choice.

8. In patients with a functional classification of Class III or IV antepartum digitalization and the relief of heart failure before the onset of labor are essential to a satisfactory outcome. In addition, the second

stage of labor should be avoided in these patients, by forceps delivery upon full dilatation of the cervix.

9. Cesarean section has a limited, although definite, place in the treatment of heart disease in pregnancy. In our series of cases, the incidence of cesarean section on the indication of heart disease has been steadily declining during the past five years, due no doubt to improved prenatal supervision and management as well as to a definite endeavor to register the cardiac patients in the special cardiac clinic as early as possible in pregnancy.

10. Sterilization, likewise, has a proper place in the management of organic heart disease. It is our practice to effect sterilization in well over one-half of the patients in Class III who are delivered by cesarean section and in all those in Class IV.

11. The maternal mortality is about twenty-five times higher in the untreated than in the treated pregnant cardiac patient. Adequate examination and evaluation of the cardiac status at the time of the patient's first visit, proper selection of candidates for therapeutic abortion, proper prenatal care in a special cardiac clinic, sufficient bed rest and hospitalization, digitalization, and the proper method of delivery are the main factors in the treated group responsible for the low maternal death rate. Mortality from heart disease in pregnancy under such a program can be almost eliminated. In such a regimen it is essential that every cardiac patient be examined before the end of the third month of gestation when a therapeutic abortion is still feasible, should such be indicated after evaluation of the cardiac status.

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## Department of Statistics\*

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### A STATISTICAL STUDY OF 500 CONSECUTIVE ABDOMINAL HYSTERECTOMIES

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SINCE the advent of a completely new regime in the department of gynecology and obstetrics at the St. Louis University group of hospitals some nine years ago, it has been our opinion that total abdominal hysterectomy is done almost to the exclusion of the supracervical operation, especially since the development of a definite operative plan.

In order to prove to ourselves that the above formulated idea was factual, we have attempted the critical study of the last 500 consecutive abdominal hysterectomies at the University hospitals.† Of these procedures, fully 80 per cent of the total operations were performed by resident gynecologists with one to two years of specialized training. Of the subtotal operations, approximately 70 per cent were done by visiting surgeons. This statement requires clarification in order to interpret properly such figures.

The greater majority of the cases presented were clinic patients. These were almost invariably operated upon by resident physicians except in those instances of extensive pathology where the member of the attending staff believed his own capabilities more suited to cope with the obstacles. By this same token, then, we can place the greater part of the mortalities under the names of fully qualified attending gynecologists, since the deaths in this series occurred most frequently in severe complicated cases. Also, carrying along on this same theme, we find a much higher mortality rate among subtotal than among total hysterectomies. This fact which, at first glance appears amazingly inconsistent, since the subtotal operation is generally regarded as technically much easier and less time consuming is, upon thorough analysis readily understood. The resident staff, together with their active preceptors, perform total hysterectomies almost routinely and, therefore, do the subtotal operation only when the condition of the patient and the pelvic and constitutional pathology warrant the less radical operation.

\*In view of the value, as matters of record, of statistical observations dealing with specific operations and procedures in institutional practice, the Editors are inaugurating this Department as a trial measure. Contributions are solicited for this purpose which shall include statistical reviews of indications, results, and other pertinent items related to the work of a particular hospital or individual in any given field.

†Wertheim operations were not included among the total hysterectomies nor were Porro operations included in the subtotal group although several of both procedures have been performed.

We believe that complete abdominal hysterectomy is little if any more time consuming than supracervical hysterectomy when a given case is not attended with untoward complicating factors. We also believe that an adequately prepared and adhered to operative plan can and does simplify the two types of operations, so that the one may be done as easily as the other. Needless to say, and this is borne out in our statistics, we do not contend that all pelvic pathology should be treated by total hysterectomy even when surgery is definitely indicated. Some pathology is grossly so overwhelming as to suggest discretion to the operator, and the few added minutes that might be required to remove a cervix in a case already potentially shocked by a prolonged procedure are not warranted. Indeed, in such fortunately rare circumstances we subscribe to the use of the supracervical operation.

Our reasons for the performance of the total operation are those brought forth by many authorities, namely:

1. That the removal of the entire organ precludes the possibility of disease in a remaining, practically useless, fragment.
2. That the cervical stump does not prevent the symptom of dyspareunia, for indeed, we do not seem to be confronted with this annoyance.
3. That the vagina, when surgery is carefully executed, is not materially shortened but rather may even be lengthened.

Before the general impression is given that our surgery is too radical let it be said that in our own minds we do not feel that such criticism is merited, particularly in view of our statistics which show that in only 45 per cent of the total hysterectomies were both adnexa removed. Actually, staff physicians train their residents in conservative gynecology.

In Table I is shown the division of the total number of cases studied and in Table II a comparison with recent figures presented by other workers.

TABLE I. DIVISION OF CASES

TYPE OF OPERATION	NUMBER	%
Total hysterectomy	419	83.8
Supracervical hysterectomy	81	16.2
Entire series	500	100.0

TABLE II. COMPARATIVE STATISTICS

AUTHORS STUDIED	TOTAL NO.	SUBTOTAL HYSTERECTOMY	MORTALITY %	TOTAL HYSTERECTOMY	MORTALITY %
Harris <sup>1</sup>	1,145	314	0.6	831	0.6
Masson <sup>2</sup>	2,542	766	0.9	1,776	1.2
Miller and Prejean <sup>3</sup>	629	255	2.75	374	1.33
Boice <sup>4</sup>	862	656	3.00	206	1.00
Weir <sup>5</sup>	1,784	348	2.30	1,436	0.76
Pearse <sup>6</sup>	1,616	1,243	3.40	373	2.90
Authors' series	500	81	3.70	419	1.43

The uncorrected mortality rate for this series was 1.80 per cent, the result of 9 deaths. This is fully explained in Table III.



TABLE III. MORTALITY RATE

	TOTAL HYSTERECTOMY	SUPRACERVICAL HYSTERECTOMY	ENTIRE GROUP
No. of deaths	6	3	9
Percentage	1.43	3.70	1.80

Three of the 6 deaths in the total hysterectomy group and 2 of the 3 in the subtotal group were the results of severely complicated operative cases. Only two cases, one from each group, are considered as deaths due to nonoperative causes. A brief résumé of the 9 fatalities is herewith appended:

1. Aged 37 years. Diagnosis: fibroid uterus with huge varicosities of the broad ligaments. Subtotal hysterectomy done. Spinal anesthesia. Died four hours later of shock and hemorrhage. This is, without question, an operative death due to inability to control the hemorrhage from the broad ligament varicosities.

2. Aged sixty-one years. Diagnosis: fibroid uterus. Complete hysterectomy with bilateral salpingo-oophorectomy done. Ether anesthesia. Operative time, 60 minutes. Died from evisceration, cachexia, and peritonitis on the sixteenth postoperative day.

3. Aged 60 years. Diagnosis: carcinoma of the fundus uteri and ventral hernia. Total hysterectomy and repair of hernia done. (The tubes and ovaries had been removed previously.) Ether anesthesia. Operative time, 240 minutes. Patient died from cardiac insufficiency and pneumonia on the fourth postoperative day. This death, in all probability, was due to the extremely prolonged operative procedure.

4. Aged 47 years. Diagnosis: sarcoma of the uterus. Complete hysterectomy performed. Operative time, 60 minutes. Ether anesthesia. Died suddenly on the twelfth postoperative day of pulmonary embolus.

5. Aged 59 years. Diagnosis: intraligamentary fibroid of the uterus. Operation, supracervical hysterectomy with bilateral salpingo-oophorectomy. Operative time, 60 minutes. Ether anesthesia. Patient died on the fourteenth postoperative day of arteriosclerotic heart disease and nephrosclerosis. This death was nonoperative in character.

6. Aged 59 years. Diagnosis: carcinoma of the right ovary. Complete hysterectomy and bilateral salpingo-oophorectomy done. Operative time, 80 minutes. Gas-ether anesthesia. Jejunostomy done for intestinal obstruction twenty-four days later, but the patient died six days thereafter.

7. Aged 25 years. Diagnosis: generalized abdominal tuberculosis with perforation of the colon and sarcoma of the right ovary. Total hysterectomy with bilateral salpingo-oophorectomy and resection of 4 inches of colon. Operative time, 90 minutes. Spinal and local anesthesia. The patient died of shock on the first postoperative day.

8. Aged 37 years. Diagnosis: hematometra. Supracervical hysterectomy and left salpingo-oophorectomy done together with packing of the pelvis to control hemorrhage from greatly dilated pelvic blood vessels. Operative time, 120 minutes. Spinal anesthesia. Death occurred on the day of the operation from shock and hemorrhage.

9. Aged 46 years. Diagnosis: fibroid uterus and chronic appendicitis. Operation, complete hysterectomy with appendectomy. Operative time, 60 minutes. Gas-ether anesthesia. Patient died on the third postoperative day from syphilitic aortitis, massive collapse of both lungs and arteriosclerotic heart disease. This is considered a nonoperative death.

The morbidity figures are admittedly rather high. The number of morbid cases in the total hysterectomy group was 156, or 37.2 per cent. For the subtotal group it was 31, or 38.2 per cent. It is highly probable that these figures can and will be reduced. We believe that a more careful preoperative study and work up of patients will aid in this problem of reducing morbidity more than any other factor with the exception of the actual operative finesse and care in handling tissues that is ever the prime requisite for satisfactory surgical results. Table IV further subdivides the morbid cases.

TABLE IV. MORBIDITY

	TOTAL HYSTERECTOMY		SUPRACERVICAL HYSTERECTOMY	
	NO.	%	NO.	%
1. 100.4° F.-101.4° F. (for 2 days)	22	13.8	5	16.1
2. 100.4° F.-more than 101.4° F. (for 2 days)	18	11.5	4	12.9
3. 100.4° F.-101.4° F. for more than 2 days	42	26.9	3	9.6
4. 100.4° F.-more than 101.4° F. for more than 2 days	74	47.4	19	62.3

Tables V and VI require no comment. Table VII reveals the number of patients given intravenous or subcutaneous fluids in the form of glucose, blood, and saline. Several patients received more than one blood transfusion and about 33 per cent of the entire group receiving glucose or saline had such therapy employed more than once. It is

TABLE V. AGE DISTRIBUTION

	TOTAL HYSTERECTOMY		SUPRACERVICAL HYSTERECTOMY	
	NO.	%	NO.	%
20-30 years	26	6.2	10	12.3
31-35 years	64	15.2	13	16.0
36-40 years	99	23.6	21	25.9
41-50 years	190	45.3	28	34.5
51-60 years	35	8.3	9	11.1
61-70 years	5	1.2	0	0.0

TABLE VI. ANESTHETICS

	TOTAL HYSTERECTOMY		SUPRACERVICAL HYSTERECTOMY	
	NO.	%	NO.	%
Gas-ether	163	38.9	42	51.8
Spinal	162	38.6	20	24.7
Ether	85	20.2	19	23.4
Spinal and ether	7	1.6	0	0.0
Spinal and local	2	0.4	0	0.0

TABLE VII. PARENTERAL FLUIDS

	TOTAL HYSTERECTOMY		SUPRACERVICAL HYSTERECTOMY	
	NO.	%	NO.	%
Glucose and saline (I.V. or S.C.)	179	42.7	45	55.6
Blood (transfusions)	51	12.1	13	16.0

noteworthy that 2 or 3 residents and a like number of attending gynecologists employed intravenous glucose, 750 c.c. to 1,000 c.c. of a 10 per cent solution in saline, after almost every laparotomy. The results following this method were not perceptibly better than in those patients given parenteral fluids only when deemed necessary.

TABLE VIII. INCIDENTAL DATA

	TOTAL HYSTERECTOMY	SUPRACERVICAL HYSTERECTOMY
Average hospital stay (postoperative)	14.82 days	15.40 days
Average time of operations	83.90 minutes	84.56 minutes

Table VIII furnishes data on the average postoperative hospital stay and the average duration of the operations from incision to skin closure. Needless to say the operative time is increased by the amount and degree of the pathology encountered. However, the personal surgical skill of various operators did not play a major role in the time consumption in these cases. Fifty to sixty minutes usually sufficed to complete a moderately uncomplicated total hysterectomy when done by the resident staff.

TABLE IX. OPERATIVE PROCEDURES

	TOTAL HYSTERECTOMY	SUPRACERVICAL HYSTERECTOMY
<i>Hysterectomy:</i>		
With bilateral salpingo-oophorectomy	131	21
With no other procedures	92	23
With unilateral salpingo-oophorectomy	58	13
With adhesiolysis and bilateral salpingo-oophorectomy	31	0
With appendectomy	18	7
With adhesiolysis and unilateral salpingo-oophorectomy	15	4
With appendectomy and unilateral salpingo-oophorectomy	14	1
With perineorrhaphy and bilateral salpingo-oophorectomy	11	0
With appendectomy and bilateral salpingo-oophorectomy	10	3
With adhesiolysis	9	2
With closure of cervix and bilateral salpingo-oophorectomy	8	0
With repair of hernia and bilateral salpingo-oophorectomy	7	1
With perineorrhaphy	6	0
With repair of intestine and bilateral salpingo-oophorectomy	5	0
With adhesiolysis, repair of hernia and unilateral salpingo-oophorectomy	2	0
With anterior and posterior colporrhaphy and bilateral salpingo-oophorectomy	1	0
With cecostomy, repair of rectum and bilateral salpingo-oophorectomy	1	0
With repair of bladder	0	4
With repair of intestine	0	1
With packing of pelvis	0	1

Table X reveals the complications that occurred while the patients were hospitalized. These, although numerous, do not entirely account for the morbidity figures of 37.2 per cent for total hysterectomy and

TABLE X. OPERATIVE COMPLICATIONS

	TOTAL HYSTERECTOMY		SUPRACERVICAL HYSTERECTOMY	
	NO.	DEATHS	NO.	DEATHS
Wound infections	23	0	7	0
Urinary infections	8	0	3	0
Shock	4	1	2	2
Pelvic abscess	4	0	0	0
Peritonitis	4	0	0	0
Vesicovaginal fistula	4	0	0	0
Thrombophlebitis	3	0	2	0
Massive collapse of lungs and atelec- tasis	3	1	0	0
Pneumonia	2	0	0	0
Cardiovascular renal disease	1	1	2	1
Evisceration	1	1	0	0
Pulmonary embolus	1	1	0	0
Intestinal obstruction	1	1	0	0
Rectovaginal fistula	1	0	0	0
Hemorrhage from vaginal cuff	1	0	0	0
Total	61	6	16	3

38.2 per cent for subtotal hysterectomy as shown fully in Table III. Doubtless the blame for a good proportion of the unexplained morbidities can be laid to a mild cystitis or pyelitis which was not diagnosed. It is practically impossible to define a subacute bladder infection unless one is constantly on guard for such a complicating factor and unless proper diagnostic measures are carried out.

TABLE XI. OPERATIVE TRAUMA

	TOTAL HYSTERECTOMY		SUPRACERVICAL HYSTERECTOMY	
	NO.	DEATHS	NO.	DEATHS
Rent in bladder (repaired)	0	0	4	0
Injury to intestine (repaired)	4	0	0	0

TABLE XII. PATHOLOGIC FINDINGS

PATHOLOGY	NUMBER
Fibromyoma of uterus	264
Chronic pelvic inflammatory disease	144
Chronic cervicitis	120
Ovarian tumors	91
a. Benign	87
b. Malignant	4
Adenomyosis	22
Uterine malignancies	19
a. Carcinoma	14
b. Sarcoma	5
Endometriosis	11

Table XII indicates the more frequently noted pathological findings. There were, also, a myriad of other findings but these occurred rarely, as for example: hematometra, hematocervix, old ruptured ectopic pregnancy, generalized abdominal tuberculosis, carcinoma of the bladder, instrumental wound of the uterus following dilatation and curettage, etc. Chronic cervicitis was the third most frequently encountered diagnosis. This probably could have been noted at least 90 per cent of the

time, but we included only those cases presenting gross pathologic changes in the cervix. The pathology noted did not differ greatly from that reported in similar articles with fibromyomas of the uterus and chronic pelvic inflammation being very frequent.

TABLE XIII. POSTOPERATIVE EXAMINATIONS

FINDINGS	TOTAL HYSTERECTOMY	SUPRACERVICAL HYSTERECTOMY
Vaginal cuff granulations	56	0
Menopausal syndrome	48	7
Wound infections	19	6
Shortened vagina	9	0
Hernias	4	1
Rectovaginal fistula	4	0
Vesicovaginal fistula	3	0
Pelvic abscess	3	0
Senile vaginitis	2	0
Dyspareunia	1	0
Frigidity	1	0
Carcinoma of the rectum	1	0
Thrombophlebitis	0	4
Cervical erosion	0	2
Carcinoma of cervix	0	1
Totals	151	21

Regarding Table XIII, we have not included cases that were symptom-free on the first postoperative examination. Two hundred and sixty-two complete hysterectomies and 57 supracervical hysterectomies were apparently completely cured at the time of the first examination which usually took place six weeks after operation. There were 9 cases in which the vagina was considered to be shortened after complete hysterectomy. However, of these only 2 revealed a total length of less than 3 inches. The other 7 patients had vaginas ranging from 3 to  $3\frac{1}{4}$  inches in length. Vaginal cuff granulations, the most frequent finding, were usually slight in degree and readily responded to therapy with caustics. Seldom did these granulations persist after 1 or 2 applications of 2 to 10 per cent silver nitrate solution.

In conclusion, we fully realize that reports of this nature have been numerous in the literature. As previously implied, we embarked upon this study for our own enlightenment and the results are, we feel, gratifying. Each case in this series was personally fully studied by us and the statistics presented are accurate as taken from the records of Firmin Desloge Hospital.

Since a large proportion of the total hysterectomies were performed by resident gynecologists with a minimum of training, and since the mortality figure of 1.43 per cent for these cases is low, we firmly believe that a given physician may be as facilely trained in the performance of total abdominal hysterectomy as in the supracervical operation and that this physician will be quite competent to perform the more radical procedure. We do not deem it necessary to campaign for the routine use of the total operation since this has been advocated for years. A definite, planned, operative technique can, with practice, give most excellent results whether that technique be directed toward the performance of total or subtotal hysterectomy.

We wish to express our deep appreciation to Dr. William H. Vogt, Sr., Director of the Department of Gynecology and Obstetrics, who has personally supervised not only a large number of these operations but also the composition of this paper.



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## Correspondence

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### Thyroid Extract and Iodine Therapy in Pregnancy Toxemia

To the Editor:

I have read with interest Dr. Colvin's article on this subject in the February, 1942, issue of the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*. There are several points upon which I would like to have clarification or make comments.

In Tables IV and V it is shown that in the two control groups of mild vascular disease (untreated), the incidence of toxemia was 14.6 and 6.1 per cent, respectively. If there can be such a great difference in the incidence of toxemia in two control groups, can the difference in the incidence of toxemia between treated and untreated cases be considered of significance?

The author does not indicate whether or not the period of observation was the same for all cases, or whether the period of treatment was comparable for all of the treated groups. No mention is made of the other forms of treatment, such as bed rest, diet, etc., that may have been recommended for the control or treated groups. These might have an important bearing on the conclusions.

There are two statements in the article that seem to be contradictory. "For some unaccountable reason, the administration of iodine to cases of vascular disease during pregnancy fails to lower the already low incidence of toxemia in these cases;" "The results indicate that the incidence of toxemia superimposed on early vascular disease is reduced 50 per cent by the use of iodine."

Table III shows 396 "normal" cases with minus basal metabolism, in the text is a statement that only those with a minus metabolism were treated, yet Table VIII shows only 273 "normal" cases received treatment. The author does not explain why the 123 remaining patients with minus basal metabolism were not treated. There are 143 "normal" cases in Table III with basal metabolic rates of 0 or plus. Presumably these would be the "normal" cases for control, yet Table VIII lists 316 "normal" control cases.

The author has made an extremely interesting study, but the evidence presented does not seem to this reader to substantiate the conclusions.

EDWIN F. DAILY, M.D.,  
*Director, Division of Health Services,  
Federal Children's Bureau.*

June 24, 1942.

### Reply by Dr. Colvin

To the Editor:

It happens too often in medical literature that tables, and conclusions drawn from them, are accepted as facts without a searching analysis being made by the reader. We are indebted to Dr. Daily for the questions and criticisms offered relative to our article.

First of all, we admitted in the paper (page 190) that, "it would have been desirable had the study covered a larger series of cases in both the thyroid and iodine treated groups, but the benefit of iodine in reducing the incidence of toxemia is so striking that we feel that a larger series of cases would not materially alter the results." Also on page 191, we expressly worded the final conclusion "*gives promise* of effecting a great reduction in the frequency of true toxemia of pregnancy," to encourage further trial of the treatment. We did not wish to imply that iodine had as yet been proved to be a specific prophylactic agent for toxemia of pregnancy.

In his comment relative to Tables IV and V, a variation of 14.6 per cent and 6.1 per cent in the control groups of 48 and 49 cases, can easily occur with a small number of cases, whereas the percentages based upon 155 and 161 cases are more reliable.

The manner of treatment and period of observation were comparable for all the treated and control groups, and we do not believe these factors have any bearing on the conclusions.

Concerning the two apparently contradictory statements referred to by Dr. Daily: If we add the nontreated mild vascular disease cases in Table IV (48) and Table V (49), we obtain 97 cases, as given in Table VII, with 10 cases of toxemia or 10.3 per cent, which is a more reliable figure. Since the iodine treated vascular disease cases (39) showed toxemia in only 5.1 per cent, our statement that "the incidence of toxemia superimposed on vascular disease is reduced 50 per cent by the use of iodine," is the correct one, rather than our statement "for some unaccountable reason the administration of iodine to cases of vascular disease during pregnancy fails to lower the already low incidence of toxemia in these cases."

His question in regard to Tables III and VIII apparently arises from the fact that he interprets normal cases as those showing plus metabolic rates, whereas we designate normal cases as those free from vascular disease.

It is our intention to bring this investigation up to date at some future time by the addition of several hundred additional cases.

E. D. COLVIN, M.D.

Atlanta, Ga., July 6, 1942.

## Editorial

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### Women in the War Effort

THE present global conflict has called into action the participation of women to a degree as never before. Not only industry but what might be designated as the supplementary combat forces have drawn upon the ranks of those who can no longer be regarded in a popular sense as the weaker sex. To make woman's participation effective as a war worker, her essentially feminine characteristics have had to be taken into account and special rules and regulations devised to protect her in the hazards of her new activities. Government and medical organizations have combined in the effort to preserve her health and well-being during a period of stress in which it has been assumed she might prove physically inferior.

Recent promulgations from official sources indicate a necessity for this enlistment of women in the war industries. The results of their labors seem to have proved of great value and their induction into factory and similar employment is believed to release many men for the combat forces. If this constitutes a part of the necessary effort to win the war, we should accept it. In doing so, however, we must divorce from the movement any possible underlying element of glamor and choose as participants those women whose entrance into labor would not disrupt their obligations toward society and the family.

Admittedly there are hazards associated with factory work which involve men less than they do women, therefore the conditions for employment of the latter must be worked out even more carefully. The ordinary requirements of general physical and mental soundness as we might term them, must be supplemented by those involved with the genital sphere. If disturbances in the latter would incapacitate or endanger or complicate employment, they must be sought out and treated. In addition, however, there are obligations to a family and small children which cannot be set aside for the mere desire to increase an income. If these obligations are overcome by providing accessory services for the purpose, will they not prove both costly and unsatisfactory in more than one sense? In addition there is the plan for providing for the special care of pregnant women in factory jobs. As a matter of fact why should pregnant women be employed at all in hazardous occupations or any others that make demands on physical resources which should be devoted to carrying out her foremost obligation to society? For years we have been developing methods to protect her during this all-important period, and now we are urging

her to expose herself to a possible interruption of her child-bearing function. Surely the supply of female labor can be augmented from other available sources, among which is that army of young women engaged in non-essential occupations, including those catering to vanities, fashions, and amusements. A greater effort to obtain recruits from such sources should be developed before invading the ranks of pregnant women to fill a possible gap. The responsibilities and strains of a factory job in a war industry should not become involved with thoughts centered on small children left at home or elsewhere, or about the outcome of a pregnancy.

This war is defined as a total war. Consequently it involves every one, perhaps indiscriminately, including men, women, and children. In our efforts, however, to bring it to a successful conclusion, we must weigh carefully what each group can do to achieve that end and in the meanwhile to preserve, so far as woman is concerned, her particular function in our social economy. This applies above all to her place as a prospective mother. *Pregnancy may eventually prove more worth while than making bullets.* Whatever problems may be involved, they demand attention and the possible solution must be based on reasoned study and not hysteria. Physically fit women, married or unmarried, and free from family ties, should, in our vast population, be found in sufficient number to rule out a resort to pregnant women in our expanded program of war industry.

## Society Transactions

### SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS

*ANNUAL MEETING AT ATLANTA, GA., FEBRUARY 6 AND 7, 1942*

The following papers were presented:

- Stricture of the Ureter in the Female.** A. J. Kelly, Savannah, Ga.
- Vitamin Studies in Vulvar Dermatoses.** Robert Greenblatt, Augusta, Ga.
- Detailed Technique of a Modified Local Anesthesia for Cesarean Section.** Alfred C. Beck, Brooklyn, N. Y. (by invitation). (For original article, see page 558.)
- Eclampsia and Ovarian Pregnancy.** C. B. Pride, Morgantown, W. Va., and M. Pierce Rucker, Richmond, Va. (For original article, see page 575.)
- Placental Polyp with Severe Late Puerperal Hemorrhage.** Charles W. Dorsey, Roanoke, Va. (For original article, see page 591.)
- Anencephalus (with Acute Hydramnios) Diagnosed by X-ray.** Waverly R. Payne, and Harvey G. Bland, Newport News, Va. (For original article, see page 593.)
- Acute Yellow Atrophy of the Liver.** C. H. Mauzy, Winston-Salem, N. C.
- Unusual Gynecologic-Obstetric History.** Robert Seibels, Columbia, S. C.
- Diaphragmatic Hernia as a Complication of Pregnancy.** A. M. Groseclose, Roanoke, Va.
- Puerperal Uterine Contractions.** William Bickers, Richmond, Va. (For original article, see page 581.)
- Comparative Measurements of the Female Pelvis.** Kenneth Dickinson and I. M. Procter, Raleigh, N. C. (For original article, see page 585.)
- The Etiologic and Pathologic Factors in a Series of 1741 Fibromyomas of the Uterus.** Richard Torpin, Edgar Pund, and W. J. Peeples, Augusta, Ga. (For original article, see page 569.)
- Utopian Obstetrics—President's Address.** R. A. Bartholomew, Atlanta, Ga. (For original article, see page 553.)



## Department of Reviews and Abstracts

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### Selected Abstracts

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#### Placenta

**Rauramo, N., and Kahanpaa, V.:** The Principal Methods of Treating Cases of Uteroplacental Apoplexy, *Acta obst. & gynec. Scandinav.* 20: 243, 1940.

The authors collected 163 cases of uteroplacental apoplexy observed at the Women's Clinic in Viipuri. These constituted an incidence of 0.7 per cent of the 22,058 obstetric cases seen at this clinic. The cases were divided into those treated obstetrically and those treated surgically. Before 1934 the treatment was conservative but following that year in an effort to improve the prognosis of the babies, the surgical line of treatment was instituted.

Among the 94 women treated conservatively, 76 per cent had spontaneous deliveries and only three had cesarean sections. Among the 69 women treated surgically, spontaneous deliveries occurred in 34 per cent and 47 per cent had cesarean sections. Vaginal operations were performed in 21 and 19 per cent, respectively. There were six deaths, of which five were in the conservative group and one in the surgical, but all of these six patients were delivered through the vagina. Four of the six women showed evidences of severe renal disease. A change in the treatment from a conservative one to a surgical one reduced the mortality of the children from 52 to 37 per cent.

Uteroplacental apoplexy is not considered as a pregnancy toxemia but indicates severe vascular changes occurring in cases of toxemia. In fatal cases, the cause of death might be hemorrhage but not a severe toxemia. Hence, the more severe cases are not suitable for cesarean section.

A follow-up was made by the author who found that uteroplacental apoplexy does not lead to sterility.

J. P. GREENHILL

**Ballin, R.:** Premature Separation of the Placenta, *Monatschr. f. Geburtsh u. Gynäk.* 112: 257, 1941.

Whereas, formerly, mechanical trauma and inflammation of the endometrium were considered to be the pathologic factors in abruptio placentae, Ballin maintains that neuropathy or blood pressure variations of unknown causes are now believed to be the chief causes of premature detachment of the placenta. In the author's series the maternal mortality was 7 per cent, but a number of women were brought to his hospital in a moribund condition. The infant mortality was 59 per cent, of which 50 per cent were either too premature to live or were already dead in utero.

J. P. GREENHILL

**Flexner, Louis B., and Gellhorn, Alfred:** *A Comparative Study of Placental Permeability*, *Anat. Rec.* 82: 411, 1942.

This study attempted to show a difference in permeability of morphologically different placentas as measured by the rate of transfer of radioactive sodium. Dividing various mammalian placentas into types, according to the numbers of layers of tissue interspersed between maternal and fetal blood, the authors were able to show an inverse correlation to the rate of transfer.

L. M. HELLMAN

**Winkler, H., and Linden, L.:** *The Change in the Treatment of Placenta Previa During the Last Forty Years*, *München. med. Wehnschr.* 88: 66, 1941.

Winkler and Linden analyzed the results of 373 cases of placenta previa observed from 1900 to 1939 in 21,724 labor cases. This represents an incidence of 1.72 per cent. The complications generally observed in cases of placenta previa were hemorrhage before and during labor, malpresentation of the fetus, atony of the uterus and post-partum hemorrhage. In this series of cases, delivery was accomplished by abdominal cesarean section in 22 per cent, by spontaneous delivery in 20.6 per cent, Braxton Hicks' version in 18.8 per cent, the use of a bag and Braxton Hicks' version in 14 per cent, and spontaneous delivery after a bag in 7.5 per cent.

In recent years the tendency has been to perform more abdominal cesarean sections in cases of placenta previa, because this operation yields the best results for both mother and child.

J. P. GREENHILL

**Rustia, Guillermo, and Tancinco, Gloria:** *Placenta Previa: Analysis of 369 Cases*, *J. Philippine Islands M. A.* 20: 649, 1940.

An analysis of 369 cases of placenta previa is presented with regard to the frequency, the maternal morbidity and mortality, the fetal mortality and the results obtained. There were in all 16 deaths in the series, a percentage of 4.33. Two women died before delivery, five died of puerperal infection, and nine died a few hours after delivery either from acute anemia or shock. Spontaneous delivery occurred in 124 cases in this series. Operative delivery was performed in the other cases.

The following tabular statement shows the results obtained: The Willet's method of operation was performed 61 times:

No. of mothers who survived	60	98.36 per cent
No. of mothers who died	1	1.63 per cent
No. of children living	19	31.14 per cent

The Braxton Hicks' version was performed 62 times:

No. of mothers who survived	58	93.54 per cent
No. of mothers who died	4	6.45 per cent
No. of children living	0	0.00 per cent

Cesarean section was performed 73 times:

No. of mothers who survived	71	97.39 per cent
No. of mothers who died	2	2.73 per cent
No. of children living	49	67.12 per cent

The Braxton Hicks' version is rapidly losing popularity in most clinics. The technical difficulties of the procedure limit its use to trained obstetricians. The Willet's method, as well as cesarean section, has its own place in the management of placenta previa.

C. O. MALAND

**Vaughn, Charles E., Weaver, R. T., and Adamson, D. L.:** Roentgenographic Visualization of the Placenta, Utilizing the Plastic Filter, *Canad. M. A. J.* 46: 314, 1942.

A brief history of placentography is given. The technical difficulties of adequate visualization are pointed out, and use of a graded plastic opaque screen described. The grading of the screen is such that, in the lateral view, more x-rays are allowed to pass through the region of the spine and pelvis than through the anterior abdomen. The results in 52 cases are excellent. Not only the anterior and posterior walls of the uterus are well visualized, but also the lower uterine segment.

J. M. HELLMAN

**Sala, Silvestre L., and Bergdolt, Enrique G.:** New Observations on the Diagnosis of Placenta Previa by Cystography, *Arch. de la clin. obst. y Ginec. "Eliseo Canton"* 1: 164, 1942.

Sala and Bergdolt have found that 25 c.c. of a 12.5 per cent solution of NaI introduced into the bladder produces a better radiogram than the 40 c.c. previously used. With the patient supine the x-rays are directed ventrodorsally; at the midpoint of the pubumbilical line; 3 sec. exposure, focal distance 76 cm., 65 kv. and 100 ma. Variations in technique such as the use of air as contrast medium and different angles of incidence of the rays have not increased the efficiency of the procedure. Normally in the eighth and ninth months of gestation, the shadows of the fetal head and the filled bladder are contiguous, although a separation up to 1 cm. is perfectly normal. The presence of the placenta between the fetal head and the shadow of the bladder causes an increase in this space. Earlier, in the seventh month, the separation in some normal cases is greater than 1 cm.

The most important causes of error in diagnosis are: opacities in the rectum, polyhydramnios and lateral flexion of the uterus, prolapse or shortness of the cord, low lying tumors, narrow pelvis and, particularly, a low lying placenta on the posterior wall of the uterus. Another important source of error may occur in cases of premature separation of the placenta when clots accumulate in the lower uterine segment.

In the 21 cases presented, the authors claim 90.5 per cent accurate diagnoses. In one of the two cases incorrectly diagnosed as placenta previa, the radiogram showed a triangular area of separation between the fetal head and the bladder, with the apex at the midline and the base toward the left at which point the separation was 21 mm. At delivery large clots were passed immediately after the fetus and before the placenta, indicating a premature separation of the placenta and probable presence of a clot in the position of the clear space in the radiogram. The second case in error was that of a patient with a generally contracted pelvis of mild degree.

The authors believe that experience permits recognition of certain causes of error before making the radiographic diagnosis and that the method can be very useful in clinical practice.

J. P. GREENHILL

**Jakob, Alfredo:** Placenta Accreta, Imminent Rupture Gravid Uterus, *Bul. Soc. de obst. y ginec. de Buenos Aires* 19: 488, 1940.

The author reviews the literature. All of the authors are of the opinion that in a previous history one finds a history of puerperal infection or curettage. In rupture of the uterus in placenta accreta, this association was verified thirteen times, and in this group eight deaths occurred. During pregnancy the symptomatology is vague. Certain pregnant women have pain, others might have slight bleeding. Mortality

was 87.5 per cent in patients not operated upon and 57 per cent in those patients operated upon. This grave complication of pregnancy according to the author should be treated only by surgery.

MARIO A. CASTALLO

**Dippel, A. Louis, and Brown, Webster H.: Direct Visualization of the Placenta by Soft-Tissue Roentgenography, New England J. Med. 223: 316, 1940.**

The authors discuss the various methods by which the placenta can be visualized and describe in detail the special usefulness of soft-tissue roentgenography. It represents a valuable aid in cases of suspected placenta previa and usually obviates the necessity of vaginal examination. The paper includes six excellent roentgenograms.

HUGO EHRENFEST

**Crainicianu, A.: The Early Diagnosis of Pregnancy by the Friedman-Brouha Reaction, Aided by Transperitoneal Ovarioscopy, Rev. franç. de gynéc. et d'obst. 35: 30, 1940.**

At the present time there are 48 tests to determine early pregnancy, but those generally employed are the Aschheim-Zondek on the mouse and the Friedman-Brouha tests on the rabbit. Both of these tests when properly performed are practically 100 per cent correct. The Friedman test is more popular because the results may be obtained in forty-eight hours. In order to diminish even this time, the author introduced the use of transperitoneal ovarioscopy. The principle of this procedure consists of examining the ovaries through a ureterscope from time to time to determine the first modifications of the Graafian follicles. The aim is to detect infrafollicular hemorrhage which is the characteristic of a positive pregnancy reaction. The author used this method in 100 cases of suspected pregnancy, of which 50 were positive. A positive reaction was recognized by this procedure in less than twenty-four hours in 80 per cent of the cases. In negative cases the ovarioscopic examinations were continued at intervals up to forty-eight hours.

J. P. GREENHILL

**Scott, William A.: The Treatment of Placenta Previa, Canad. M. A. J. 42: 442, 1940.**

The author analyzed a series of 81 patients with placenta previa at the Toronto General Hospital. Of these, 17 were complete and 64 incomplete. Two maternal deaths occurred. The fetal mortality rate was 40 per cent which, when reduced by nonviable, macerated, and deformed fetuses became 28.4 per cent. He emphasizes that all cases should be treated in the hospital and that many of the emergencies could be avoided if the significance of the first bleeding was appreciated. Cesarean section should not be routine but is the safest method in nearly all cases of complete placenta previa. The hydrostatic bag has a place in the management of properly selected cases. Version is a valuable method of treatment for emergency cases which may have to be treated in the home.

CARL P. HUBER

**Caldera, R.: Placenta Previa. A Review of 251 Cases, J. Obst. & Gynaec., Brit. Emp. 46: 531, 1939.**

Caldera reports 251 cases of placenta previa in 26,116 labors, an incidence of one in 104 labors.

During the last four years there were 199 cases of placenta previa with 23 deaths, giving a maternal mortality of 11.5 per cent.

Of the 23 deaths, 11 occurred before delivery; in 6 of these, death could be attributed solely to hemorrhage, while in the remaining five cases shock following podalic version was an important contributory factor. In the case of the 12 patients whose deaths occurred after delivery, 3 were due to puerperal sepsis; with regard to the remaining 9, shock following podalic version in 8 cases and delivery by the forceps in one case were responsible for the fatal issue. Thus in no less than 20 cases the cause of death was hemorrhage complicated by shock.

In a country like Ceylon, where malaria and ankylostomiasis are endemic, the majority of patients are anemic and ill-nourished, and in such patients even a small hemorrhage may lead to serious results. Moreover, many patients seek hospital treatment after they have had repeated hemorrhages.

The percentage of stillbirths for the central, marginal, and lateral varieties is 69.6, 49.4, and 45, respectively.

Podalic version was the method of treatment adopted in 87 cases. The maternal mortality was 17.2 per cent and the fetal mortality 74 per cent. In 13 cases of breech presentation when a leg was brought down, the maternal mortality was 7.7 per cent and fetal mortality 69.2 per cent.

Cesarean section is the safest method of delivery for both the mother and the child. Only 5 patients were treated by this method, with no maternal nor fetal deaths. The membranes were ruptured artificially on 38 occasions. There were no maternal deaths and the fetal mortality was 39.4 per cent.

J. P. GREENHILL

**Fleming, John G.: Premature Separation of the Normally Implanted Placenta. A Study of 72 Cases, J. Medicine 20: 271, 1939.**

A study of 72 cases of premature separation of the normally implanted placenta revealed (University of Cincinnati) an incidence of separation of 1 in 57.5 cases in the general deliveries, and of 1 in 14 cases in the special toxic-hypertensive-nephritic syndrome. Within this toxic group of cases, separation occurred four times as often as in the general deliveries, and one and one-half times as often as eclampsia.

Toxemia was a complication in 48, or 66.6 per cent, of the cases. Some aspect of the toxic-hypertensive state, often of a severe degree, was present in the majority of the cases complicated by internal hemorrhage and of those resulting in fetal and maternal deaths.

The high incidence of the condition in youthful patients of low parity may possibly indicate a predisposition in certain individuals to the toxic-hypertensive-vascular disease process. This predisposition may also account for the frequent association of the more severe cases with repeated pregnancies and advancing years.

There is considerable evidence that, in the majority of cases, a general vascular or arteriolar spastic damage, now recognized as the pathologic process underlying the toxic and eclamptic states, is also active in the uterus in infarction of the placenta and in partial and complicated separation of the placenta.

Three maternal deaths and 29 fetal deaths, a rate of 4.2 and 40.3 per cent, respectively, followed delivery of six patients from above and 66 from below. Conservative management results in one maternal death, a rate of 1.5 per cent in the 66 patients delivered from below.

J. P. GREENHILL

**Pohl, A.: What Value Has the Prophylactic Administration of Prontosil in Cases of Manual Removal of the Placenta, Med. Klin. 35: 346, 1939.**

In a series of 46 cases of manual removal of the placenta, the author found that the prophylactic use of prontosil prevented serious infection in the puerperium.



The women in this series were discharged from the hospital as early as women who had normal labors provided they were not too anemic. The author advises the intra-gluteal administration of prontosil immediately after delivery to all women in whom there is likelihood that infection will set in after labor. In addition prontosil tablets should be given during the first four days.

J. P. GREENHILL

**Browne, F. J.: Danger of Willett's Forceps in Placenta Previa, Proc. Roy. Soc. Med. 32: 1209, 1939.**

Since its first description, in 1925, the Willett forceps has been used in 252 instances among 3,103 cases of placenta previa in 11 teaching hospitals of Great Britain. Maternal mortality amounted to 3.5 per cent and fetal mortality to 46.4 per cent. The forceps inevitably produces a more or less lacerated wound on the fetal scalp which may become infected by vaginal bacteria. The likelihood of infection is increased by death of the fetus and delay of delivery after application of the forceps—two unfavorable conditions often present in placenta previa cases.

The author reports two observations of Welch bacillus infection following the use of the Willett forceps.

HUGO EHRENFEST

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## Item

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### American Board of Obstetrics and Gynecology

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Saturday, February 13, 1943, at 2 P.M. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year. All applications must be in the office of the Secretary by November 16, 1942.

Effective this year there will be only one general classification of candidates, all now being required to have been out of medical school not less than eight years, having in that time completed an approved one year general rotating internship and at least three years of approved special formal training, or its equivalent, in the seven years following the interne year. This Board's requirements for internships and special training are similar to those of the American Medical Association since the Board and the A. M. A. are at present cooperating in a survey of acceptable institutions. All candidates must be full citizens of the United States or Canada before being eligible for admission to examinations.

All candidates will be required to take the Part I examination, which consists of a written examination and the submission of twenty-five (25) case history abstracts, and the Part II examination (oral-clinical and pathology examination). The Part I examination will be arranged so that the candidate may take it at or near his place of residence, while the Part II examination will be held late in May, 1943, in that city nearest to the largest group of applicants. Time and place of this latter will be announced later.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

## ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES\*

(Appears in January, April, July, October)

- American Gynecological Society.** *President*, George W. Kosmak, New York, N. Y. *Secretary*, H. C. Taylor, Jr., 830 Park Ave., New York, N. Y. Annual meeting, May, 1943.
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons.** *President*, W. R. Cooke, Galveston, Texas. *Secretary*, James R. Bloss, 418 11th Street, Huntington, W. Va. Annual meeting, September, 1943.
- Central Association of Obstetricians and Gynecologists.** *President*, John H. Moore, Grand Forks, N. D. *Secretary-Treasurer*, W. F. Mengert, Iowa City, Iowa. Next meeting, Des Moines, Ia., October, 1942. (Postponed.)
- South Atlantic Association of Obstetricians and Gynecologists.** *President*, Oren Moore, Charlotte, N. C. *Secretary*, T. J. Williams, University, Va. Next meeting, February, 1943, Southern Pines, N. C.
- A. M. A. Section on Obstetrics and Gynecology.** *Chairman*, L. E. Phaneuf. *Secretary*, Philip F. Williams, 2206 Locust St., Philadelphia, Pa. Next meeting. (Undecided.)
- New York Obstetrical Society.** *President*, Henry T. Burns, *Secretary*, Ralph A. Hurd, 37 E. 64th Street, New York City. Second Tuesday, from October to May, Yale Club.
- Obstetrical Society of Philadelphia.** *President*, John C. Hirst. *Secretary*, James P. Lewis, 3815 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.
- Chicago Gynecological Society.** *President*, Edward Allen. *Secretary*, Eugene A. Edwards, 104 S. Michigan Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.
- Brooklyn Gynecological Society.** *President*, Bruce A. Harris. *Secretary*, John J. Madden, 362 Washington, Ave., Brooklyn N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Avenue, Brooklyn, N. Y.
- Baltimore Obstetrical and Gynecological Society.** *President*, Lawrence Warton. *Secretary-Treasurer*, John W. Haws, 9 East Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Building.
- Cincinnati Obstetrical Society.** *President*, Edward Friedman. *Secretary*, Carroll J. Fair, Cincinnati, Ohio. Third Thursday of each month.
- Louisville Obstetrical and Gynecological Society.** *President*, Layman A. Gray. *Secretary*, E. P. Solomon, Hegburn Building, Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.
- Portland Society of Obstetrics and Gynecology.** *President*, Howard Stearns. *Secretary*, William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.
- Pittsburgh Obstetrical and Gynecological Society.** *President*, J. L. Gilmore. *Secretary*, Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.
- Obstetrical Society of Boston.** *President*, Thos. Almy, Fall River, Mass. *Secretary*, Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.
- New England Obstetrical and Gynecological Society.** *President*, Frederick L. Good. *Secretary*, R. J. Heffernan, 475 Commonwealth Avenue, Boston, Mass. Meetings held in May and December.
- Pacific Coast Obstetrical and Gynecological Society.** *President*, T. Floyd Bell. *Secretary-Treasurer*, William Benbow Thompson, 6253 Hollywood Boulevard, Los Angeles, Calif. Next meeting, San Francisco, Calif., November, 1942.
- Washington Gynecological Society.** *President*, John Warner. *Secretary*, L. L. Cockerille, 900 17th Street, N. W., Washington, D. C. Fourth Saturday, October to May.

\*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL.

- New Orleans Obstetrical and Gynecological Society.** *President*, E. L. Zander. *Secretary*, Eugene Countiss, 921 Canal St., New Orleans, La. Meetings held every other month.
- St. Louis Gynecological Society.** *President*, S. A. Weintraub. *Secretary*, Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Second Thursday, October, December, February, and April.
- San Francisco Gynecological Society.** *President*, T. Henshaw Kelly. *Secretary*, R. Glenn Craig, 490 Post Street, San Francisco, Calif. Regular meetings held second Friday in month, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.
- Texas Association of Obstetricians and Gynecologists.** *President*, Roy Grogan. *Secretary*, J. McIver, 714 Medical Arts Building, Dallas, Texas.
- Michigan Society of Obstetricians and Gynecologists** (formerly the Detroit Obstetrical and Gynecological Society). *President*, H. C. Walser. *Secretary*, Harold C. Mack, 955 Fischer Bldg., Detroit, Mich. Meeting first Tuesday of each month from October to May (inclusive).
- Obstetric Society of Syracuse Hospitals.** *President*, Edward C. Hughes. *Secretary*, Nathan N. Cohen, 713 East Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.
- Alabama Association of Obstetricians and Gynecologists.** *President*, T. M. Boulware, Birmingham, Ala. *Secretary*, Eva F. Dodge, Montgomery, Ala. Next meeting Montgomery, Ala., April, 1942.
- San Antonio Obstetric Society.** *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Texas. Meetings held first Tuesday of each month at Gunter Hotel.
- Seattle Gynecological Society.** *President*, Glen N. Rotten. *Secretary*, R. Philip Smith, 1305 Fourth Avenue. Meetings third Wednesday.
- Denver Obstetrical and Gynecological Society.** *Secretary*, Emmett A. Mechler, 1612 Tremont St., Denver, Colo.
- Wisconsin Society of Obstetrics and Gynecology.** *President*, Roland S. Cron. *Secretary*, Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

## Books Received

**PRINCIPLES OF EXTRAPERITONEAL CAESAREAN SECTION.** By James V. Ricci, M.D., Associate Clinical Professor of Gynaecology and Obstetrics, New York Medical College, etc., and James Pratt Marr, M.D., Associate Attending Surgeon, Women's Hospital in the State of New York, etc. 47 illustrations, 224 pages. Blakiston Company, Philadelphia, 1942.

**SEROLOGY IN SYPHILIS CONTROL.** With an Appendix for Health Officers and Industrial Physicians. By Reuben L. Kahn, M.S., D.Sc., Director of Clinical Laboratories and of Serologic Consultation Service of University of Michigan Hospital, etc. 206 pages. The Williams & Wilkins Company, Baltimore, 1942.

**ENDOCRINOLOGY.** Clinical Application and Treatment. By August A. Werner, M.D., Assistant Professor of Internal Medicine, St. Louis University School of Medicine, etc. Second edition, thoroughly revised. Illustrated with 327 engravings and a colored plate. 924 pages. Lea & Febiger, Philadelphia, 1942.

**LEADERS OF MEDICINE.** Biographical Sketches of Outstanding American and European Physicians. By Solomon R. Kagan, M.D. 176 pages, four illustrations. The Medico-Historical Press, Boston, Mass., 1941.

**TABER'S CYCLOPEDIA MEDICAL DICTIONARY.** By Clarence Wilbur Taber and Associates. 273 illustrations, second edition. F. A. Davis Company, Philadelphia, 1942.